Clinical trial results:
The efficacy and safety of olmesartan medoxomil/amlodipine fixed combination in patients with grade 1 to grade 2 arterial hypertension. An international randomized, double-blind, 10-week multi-factorial clinical study.

Summary

EudraCT number	2014-003470-17
Trial protocol	DE HU RO
Global end of trial date	10 October 2015

Results information

Result version number	v1 (current)
This version publication date	27 October 2016
First version publication date	27 October 2016
Summary attachment (see zip file)	Summary of Integrated clinical study report (KKL172014_CSR_Integrated Summary_160616.pdf)

Trial information

Trial identification

Sponsor protocol code	KKL172014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Krka, d. d., Novo mesto
Sponsor organisation address	Šmarješka cesta 6, Novo mesto, Slovenia, 8501
Public contact	Infopoint KKL172014, Krka, d.d. Novo mesto, +386 73312111, info@krka.biz
Scientific contact	Infopoint KKL172014, Krka, d.d. Novo mesto, +386 14751489, Clinical.trials@krka.biz

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 October 2015
Global end of trial reached?	Yes
Global end of trial date	10 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective is to compare the treatment effect of fixed-dose combinations of olmesartan medoxomil/amlodipine (TIMP) to those of the component monotherapies (RIMPs) and placebo in subjects with grade 1 or grade 2 arterial hypertension. Within the primary objective the superiority of the treatment effect of TIMPs over each RIMP of respective strength and placebo is expected to be demonstrated.

Protection of trial subjects:

This study was conducted in accordance with the Note for Guidance on GCP, the general guidelines indicated in the Declaration of Helsinki and all applicable regulatory requirements. Before initiating the study, the written and dated approvals/favorable opinions were obtained from the competent national Ethical Committees for the study protocol, amendments, and the informed consent form (ICF). Investigators explained the benefits and risks of study participation to each subject or the subject's legal representative. Written informed consent was obtained before the subject entered the study and before initiation of any study-related procedure.
During the active treatment phase, there was a possibility of rescue medication in case of marked lack of efficacy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 2015
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	Poland: 328
Country: Number of subjects enrolled	Romania: 418
Country: Number of subjects enrolled	Germany: 96
Country: Number of subjects enrolled	Hungary: 155
Worldwide total number of subjects	997
EEA total number of subjects	997

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)	811
From 65 to 84 years	186
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At the screening visit, subjects' eligibility was assessed after ICF signature. Eligible subjects were enrolled in 2-week washout/ placebo run-in period (Period I). Overall 997 subjects were screened.

Period 1

Period 1 title	Washout/run-in period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Placebo

Arm description:

This was a pre-randomization period. All enrolled subjects were assigned to this placebo arm prior to randomization.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Plac
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Number of subjects in period 1	Placebo
Started	997
Completed	841
Not completed	156
Consent withdrawn by subject	41
Adverse event, non-fatal	13
Inclusion/Exclusion criteria violation	97
Other	3
Lost to follow-up	2

Period 2

Period 2 title	Active treatment period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The study blind is assured by encapsulation of all the IMPs in identical test capsules. The identity of the IMP is not revealed on the labels.

Arms

Are arms mutually exclusive?	Yes
Arm title	OA 20/5

Arm description: -

Arm type	Experimental
Investigational medicinal product name	olmesartan medoxomil 20 mg/amlodipine 5 mg
Investigational medicinal product code	OA 20/5
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One Olmesartan medoxomil/amlodipine 20/5 mg encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Arm title	OA 40/5

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Olmesartan medoxomil/amlodipine 40/5 mg film-coated tablets
Investigational medicinal product code	OA 40/5
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One Olmesartan medoxomil/amlodipine 40/5 mg encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Arm title	OA 40/10

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Olmesartan medoxomil/amlodipine 40/10 mg film-coated tablets
Investigational medicinal product code	OA 40/10
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One Olmesartan medoxomil/amlodipine 40/10 mg encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Arm title	Olmesartan 20

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Olmesartan 20 mg
Investigational medicinal product code	O20
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One olmesartan medoxomil 20 mg encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Arm title	Olmesartan 40

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Olmesartan medoxomil 40 mg
Investigational medicinal product code	O40
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One olmesartan medoxomil 40 mg encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Arm title	Amlodipine 5

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Amlodipine 5 mg
Investigational medicinal product code	A5
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One amlodipine 5 mg encapsulated tablet administered once daily at about the same time each day, orally.

Arm title	Amlodipine 10

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Amlodipine 10 mg
Investigational medicinal product code	A10
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One amlodipine 10 mg encapsulated tablet administered once daily at about the same time each day, orally.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Plac
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo encapsulated film-coated tablet administered once daily at about the same time each day, orally.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 was a washout/placebo run-in period, during which all enrolled subjects received placebo prior to
randomization. Baseline period was Period II, during which all randomized patients received active treatment or placebo.

Number of subjects in period 2[2]	OA 20/5	OA 40/5	OA 40/10
Started	129	130	129
Completed	124	125	125
Not completed	5	5	4
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	2	-	-
Other	-	1	-
Lost to follow-up	-	-	1
Protocol deviation	3	4	1

Number of subjects in period 2[2]	Olmesartan 20	Olmesartan 40	Amlodipine 5
Started	97	96	97
Completed	93	92	94
Not completed	4	4	3
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	3	1	-
Other	-	-	1
Lost to follow-up	-	-	1
Protocol deviation	-	3	1

Number of subjects in period 2[2]	Amlodipine 10	Placebo
Started	98	65
Completed	86	61
Not completed	12	4
Consent withdrawn by subject	4	3
Adverse event, non-fatal	3	-
Other	3	-
Lost to follow-up	-	-
Protocol deviation	2	1

Notes:

[2] - 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: The baseline period was Period II, during which all randomized patients (841 in total) received active treatment.
Not all enrolled patients (997 in total) were randomized.

Baseline characteristics

Reporting groups	
Reporting group title	OA 20/5
Reporting group description: -	
Reporting group title	OA 40/5
Reporting group description: -	
Reporting group title	OA 40/10
Reporting group description: -	
Reporting group title	Olmesartan 20
Reporting group description: -	
Reporting group title	Olmesartan 40
Reporting group description: -	
Reporting group title	Amlodipine 5
Reporting group description: -	
Reporting group title	Amlodipine 10
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	OA 20/5	OA 40/5	OA 40/10
Number of subjects	129	130	129
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	109	104	107
From 65-84 years	20	26	22
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.6	55	52.3
standard deviation	± 11.1	± 10.8	± 11.7
Gender categorical Units: Subjects			
Female	58	54	61
Male	71	76	68
Previous antihypertensive therapy Units: Subjects			
Received previous AH therapy	75	75	68
No previous AH therapy	54	55	61
Smoking Units: Subjects			

Non-smokers	100	107	103
Regular smokers	29	23	26

Mean baseline SeDBP			
Units: mmHg			
arithmetic mean	96.9	97.3	97.5
standard deviation	± 4.3	± 4.5	± 4.8
Mean baseline SeSBP			
Units: mmHg			
arithmetic mean	152.1	153.3	154.2
standard deviation	± 10.9	± 13.1	± 12.4

Reporting group values	Olmesartan 20	Olmesartan 40	Amlodipine 5
Number of subjects	97	96	97
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	77	76	80
From 65-84 years	20	20	17
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	54.7	54.6	53.9
standard deviation	± 10.9	± 10.8	± 11
Gender categorical			
Units: Subjects			
Female	48	44	48
Male	49	52	49
Previous antihypertensive therapy			
Units: Subjects			
Received previous AH therapy	51	52	50
No previous AH therapy	46	44	47
Smoking			
Units: Subjects			
Non-smokers	83	79	77
Regular smokers	14	17	20
Mean baseline SeDBP			
Units: mmHg			
arithmetic mean	97.8	97.2	97.5
standard deviation	± 4.8	± 4.8	± 4.6
Mean baseline SeSBP			
Units: mmHg			
arithmetic mean	153.2	152.8	154.3
standard deviation	± 10.9	± 10.4	± 10.4

Reporting group values	Amlodipine 10	Placebo	Total
Number of subjects	98	65	841
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	82	56	691
From 65-84 years	16	9	150
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.1	53.6	
standard deviation	± 11	± 9.6	-
Gender categorical Units: Subjects			
Female	47	24	384
Male	51	41	457
Previous antihypertensive therapy Units: Subjects			
Received previous AH therapy	55	42	468
No previous AH therapy	43	23	373
Smoking Units: Subjects			
Non-smokers	79	53	681
Regular smokers	19	12	160
Mean baseline SeDBP Units: mmHg			
arithmetic mean	97.1	96.6	
standard deviation	± 4.6	± 4.1	-
Mean baseline SeSBP Units: mmHg			
arithmetic mean	153.1	152.2	
standard deviation	± 11.3	± 11.7	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
This was a pre-randomization period. All enrolled subjects were assigned to this placebo arm prior to randomization.	
Reporting group title	OA 20/5
Reporting group description: -	
Reporting group title	OA 40/5
Reporting group description: -	
Reporting group title	OA 40/10
Reporting group description: -	
Reporting group title	Olmesartan 20
Reporting group description: -	
Reporting group title	Olmesartan 40
Reporting group description: -	
Reporting group title	Amlodipine 5
Reporting group description: -	
Reporting group title	Amlodipine 10
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
FAS was defined as all randomized subjects who completed the placebo run-in period and received at least one dose of the study medication during the double-blind period, with both baseline value and at least one post-baseline value of efficacy assessment.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT was defined as all randomized subjects who completed the placebo run-in period.	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
The PP was defined as all randomized subjects without major protocol violations who receive study-directed treatment and have all assessments for all efficacy endpoints during the study.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety set was defined as all randomized subjects who received at least one dose of the study medication during the double-blind period.	

Primary: Mean change from baseline in SeDBP at week 8

End point title	Mean change from baseline in SeDBP at week 8
End point description:	
For each combination it was required to show its superiority over the respective monotherapies and placebo. Three families of hypotheses were formed based on active monocomponent's strengths (first family included highest strengths; third family included lowest strengths). In order to continue with the next family of hypotheses all null hypotheses in the previous family had to be rejected. Since not all the null hypotheses in the first family were rejected, the further hypothesis testing could not be evaluated. Therefore only the first family results are presented.	

End point type	Primary

End point timeframe:

Start and end of active treatment period (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: mmHg				
least squares mean (confidence interval 95%)	-12.8 (-14 to 11.5)	-15.5 (-16.9 to 14.1)	-13.4 (-14.9 to 12)	-11.1 (-12.7 to -9.5)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: mmHg				
least squares mean (confidence interval 95%)	-14.6 (-16.4 to 12.9)	-12.1 (-13.7 to 10.5)	-12.8 (-14.5 to 11.2)	-6.1 (-8.5 to -3.8)

Statistical analyses

Statistical analysis title	Treatment difference OA 40/10 vs PLAC
Comparison groups	Placebo v OA 40/10
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.39
upper limit	-4.6

Statistical analysis title	Treatment difference A10 vs PLAC
Comparison groups	Placebo v Amlodipine 10

Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	-2.91

Statistical analysis title	Treatment difference OA 40/10 vs O40
Comparison groups	OA 40/10 v Olmesartan 40
Number of subjects included in analysis	225
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.494
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	2.81

Statistical analysis title	Treatment difference OA 40/10 vs A10
Comparison groups	OA 40/10 v Amlodipine 10
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.155
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.66
upper limit	0.58

Statistical analysis title	Treatment difference O40 vs PLAC

Comparison groups	Placebo v Olmesartan 40
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.24
upper limit	-5.2

Secondary: Mean change from baseline in SeSBP at week 8

End point title	Mean change from baseline in SeSBP at week 8

End point description:

As for the primary efficacy endpoint, three families of hypotheses were formed based on active monocomponent's strengths (first family included highest strengths; third family included lowest strengths). In order to continue with the next family of hypotheses all null hypotheses in the previous family had to be rejected. Since not all the null hypotheses in the first family were rejected, the further hypothesis testing could not be evaluated. Therefore only the first family results are presented.

End point type	Secondary

End point timeframe:

Start and end of active treatment period (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: mmHg				
least squares mean (confidence interval 95%)	-20.7 (-23.3 to -18.2)	-22.6 (-25.4 to -19.7)	-20.6 (-23.1 to -18.1)	-18.9 (-21.3 to -16.5)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: mmHg				
least squares mean (confidence interval 95%)	-19.9 (-23.1 to -16.7)	-17.5 (-19.6 to -15.3)	-20.6 (-23.2 to -17.9)	-9 (-11.8 to -6.1)

Statistical analyses

Statistical analysis title	Treatment difference OA 40/10 vs PLAC
Comparison groups	OA 40/10 v Placebo
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-10.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.31
upper limit	-6.91

Statistical analysis title	Treatment difference O40 vs PLAC
Comparison groups	Placebo v Olmesartan 40
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-10.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.86
upper limit	-7.06

Statistical analysis title	Treatment difference A10 vs PLAC
Comparison groups	Placebo v Amlodipine 10
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	-5.92

Statistical analysis title	Treatment difference OA 40/10 vs O40
Comparison groups	OA 40/10 v Olmesartan 40
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.833
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	3.62

Statistical analysis title	Treatment difference OA 40/10 vs A10
Comparison groups	OA 40/10 v Amlodipine 10
Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.07
upper limit	2.57

Secondary: Mean change from baseline in SeDBP at week 2	
End point title	Mean change from baseline in SeDBP at week 2
End point description:	

End point type	Secondary
End point timeframe:	
From start of active treatment (baseline) to week 2	

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: mmHg				
least squares mean (confidence interval 95%)	-10.5 (-11.8 to -9.2)	-11.4 (-12.5 to -10.2)	-9.6 (-11.2 to -8)	-9.7 (-11.3 to -8.1)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: mmHg				
least squares mean (confidence interval 95%)	-10.3 (-12 to -8.6)	-8.8 (-10.2 to -7.3)	-10.1 (-11.6 to -8.7)	-4.3 (-6.3 to -2.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in SeDBP at week 4

End point title	Mean change from baseline in SeDBP at week 4

End point description:

End point type	Secondary

End point timeframe:

From start of active treatment (baseline) to week 4

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: mmHg				
least squares mean (confidence interval 95%)	-12.8 (-13.9 to -11.6)	-14.2 (-15.4 to -13.1)	-12.3 (-13.7 to -10.9)	-11.4 (-13 to -9.8)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: mmHg				
least squares mean (confidence interval 95%)	-12.9 (-14.7 to -11.1)	-10.6 (-12.1 to -9)	-11.5 (-13.1 to -10)	-6.5 (-8.6 to -4.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in SeSBP at week 2

End point title	Mean change from baseline in SeSBP at week 2

End point description:

End point type	Secondary

End point timeframe:

From start of active treatment (baseline) to week 2

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: mmHg				
least squares mean (confidence interval 95%)	-15.7 (-17.8 to -13.5)	-16.5 (-18.5 to -14.4)	-14 (-16.3 to -11.7)	-13.1 (-15.6 to -10.6)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: mmHg				
least squares mean (confidence interval 95%)	-13.4 (-16.7 to -10.1)	-11.8 (-14.1 to -9.6)	-17.1 (-21.1 to -16.2)	-5.5 (-8.3 to -2.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in SeSBP at week 4

End point title	Mean change from baseline in SeSBP at week 4

End point description:

End point type	Secondary

End point timeframe:

From start of active treatment (baseline) to week 4

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: mmHg				
least squares mean (confidence interval 95%)	-19.7 (-22 to -17.5)	-20.6 (-22.8 to -18.5)	-19.8 (-22.3 to -17.2)	-17.5 (-19.9 to -15)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: mmHg				
least squares mean (confidence interval 95%)	-16.4 (-19.6 to -13.3)	-15.7 (-18 to -13.4)	-18.6 (-21.1 to -16.2)	-8.9 (-11.7 to -6.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with SeSBP reduction from baseline ≥ 20 mm Hg at week 8

End point title	Proportion of subjects with SeSBP reduction from baseline ≥ 20 mm Hg at week 8

End point description:

End point type	Secondary

End point timeframe:

Start and end of active treatment period (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: Subjects	64	74	64	49

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: Subjects	53	42	50	13

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	828			
Units: Subjects	409			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with SeDBP reduction from baseline ≥ 10 mm Hg at week 8

End point title	Proportion of subjects with SeDBP reduction from baseline ≥ 10 mm Hg at week 8

End point description:

End point type	Secondary

End point timeframe:

Start and end of active treatment period (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: Subjects	85	99	83	55

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: Subjects	66	55	59	18

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	828			
Units: Subjects	520			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with BP goal of less than 140/90 mmHg at week 2

End point title	Proportion of subjects with BP goal of less than 140/90 mmHg at week 2

End point description:

End point type	Secondary

End point timeframe:

From start of active treatment (baseline) to week 2.

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: Subjects	60	75	52	42

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: Subjects	48	41	43	9

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	828			
Units: Subjects	370			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with BP goal of less than 140/90 mmHg at week 4

End point title	Proportion of subjects with BP goal of less than 140/90 mmHg at week 4

End point description:

End point type	Secondary

End point timeframe:

From start of active treatment (baseline) to week 4

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: Subjects	89	93	77	59

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: Subjects	59	59	53	21

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	828			
Units: Subjects	510			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with BP goal of less than 140/90 mmHg at week 8

End point title	Proportion of subjects with BP goal of less than 140/90 mmHg at week 8

End point description:

End point type	Secondary

End point timeframe:

From start to end of active treatment (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	128	127	97
Units: Subjects	89	97	81	59

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	94	65
Units: Subjects	64	68	66	23

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	828			
Units: Subjects	547			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in average 24-hour SBP at week 8

End point title	Mean change from baseline in average 24-hour SBP at week 8

End point description:

End point type	Secondary

End point timeframe:

From start to end of active treatment (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	54	52	42
Units: mmHg				
least squares mean (confidence interval 95%)	-15.3 (-18.9 to -11.7)	-13.9 (-18.9 to -8.9)	-14.6 (-19 to -10.2)	-12.3 (-16.7 to -7.9)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	46	38	25

Units: mmHg				
least squares mean (confidence interval 95%)	-16.3 (-21 to -11.6)	-6 (-10.9 to -1.1)	-16.9 (-22.1 to -11.8)	-1.2 (-8.2 to 5.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in average 24-hour DBP at week 8

End point title	Mean change from baseline in average 24-hour DBP at week 8

End point description:

End point type	Secondary

End point timeframe:

From start to end of active treatment (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	54	52	42
Units: mmHg				
least squares mean (confidence interval 95%)	-9.1 (-12 to -6.3)	-8.6 (-11.6 to -5.6)	-9.4 (-12.4 to -6.5)	-8.7 (-11.8 to -5.6)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	46	38	25
Units: mmHg				
least squares mean (confidence interval 95%)	-12 (-15.2 to -8.7)	-4.9 (-8 to -1.8)	-8.7 (-11.9 to -5.4)	-0.8 (-4.4 to 2.7)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: A number/percent of subjects unable to finish the clinical assessment due to clinically significant adverse reaction

End point title	A number/percent of subjects unable to finish the clinical assessment due to clinically significant adverse reaction

End point description:

End point type	Other pre-specified

End point timeframe:
From start to end of active treatment (baseline, week 8).

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: Subject	2	0	0	3

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: Subject	1	0	3	0

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	841			
Units: Subject	9			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change from baseline in AST at week 8

End point title	Mean change from baseline in AST at week 8

End point description:

End point type	Other pre-specified

End point timeframe:
From start to end of active treatment (baseline, week 8).

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: U/L				
arithmetic mean (standard deviation)	0 (± 9.7)	-0.8 (± 7.9)	-0.9 (± 11.6)	-0.6 (± 8.5)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: U/L				
arithmetic mean (standard deviation)	1 (± 7.2)	1.6 (± 11.5)	-1.5 (± 9.4)	-0.4 (± 8.3)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change from baseline in ALT at week 8

End point title	Mean change from baseline in ALT at week 8

End point description:

End point type	Other pre-specified

End point timeframe:

From start to end of active treatment (baseline, week 8)

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: U/L				
arithmetic mean (standard deviation)	0 (± 13.2)	0.7 (± 16.8)	-0.9 (± 16.6)	-0.2 (± 11.1)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: U/L				
arithmetic mean (standard deviation)	0.9 (± 14.4)	4.2 (± 18.9)	-2.4 (± 13.7)	0.7 (± 12.1)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change from baseline in Serum Creatinine at week 8

End point title	Mean change from baseline in Serum Creatinine at week 8

End point description:

End point type	Other pre-specified

End point timeframe:

From start to end of active treatment (baseline, week 8).

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: umol/L				
arithmetic mean (standard deviation)	2.2 (± 12.5)	1.1 (± 12.8)	0.3 (± 12.8)	0.9 (± 11.5)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: umol/L				
arithmetic mean (standard deviation)	1.1 (± 13.4)	2.6 (± 15.2)	2 (± 11.8)	1.5 (± 12.7)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change from baseline in Serum Urea at week 8

End point title	Mean change from baseline in Serum Urea at week 8

End point description:

End point type	Other pre-specified

End point timeframe:

From start to end of active treatment (baseline, week 8).

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: mmol/L				
arithmetic mean (standard deviation)	0.4 (± 2.6)	0.3 (± 3.7)	-0.3 (± 3.9)	-0.3 (± 3.5)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: mmol/L				
arithmetic mean (standard deviation)	0.8 (± 3.3)	-0.7 (± 2.5)	-0.3 (± 2.8)	-0.1 (± 1.8)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change from baseline in Serum Potassium at week 8

End point title	Mean change from baseline in Serum Potassium at week 8

End point description:

End point type	Other pre-specified

End point timeframe:

From start to end of active treatment (baseline, week 8).

End point values	OA 20/5	OA 40/5	OA 40/10	Olmesartan 20
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	130	129	97
Units: mmol/L				
arithmetic mean (standard deviation)	0 (± 0.5)	0.1 (± 0.5)	0 (± 0.5)	0.1 (± 0.6)

End point values	Olmesartan 40	Amlodipine 5	Amlodipine 10	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	98	65
Units: mmol/L				
arithmetic mean (standard deviation)	0 (± 0.6)	0.1 (± 0.9)	0.1 (± 0.6)	0 (± 0.5)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 10 weeks (from ICF signature to the end of trial).	
Adverse event reporting additional description:	
All randomised subjects who received at least one dose of study medication during the double-blind period were included in the Safety set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	OA 20/5
Reporting group description:	
Participants who received OA 20/5 along the entire active treatment period.	
Reporting group title	OA 40/5
Reporting group description:	
Participants who received OA 40/5 along the entire active treatment period.	
Reporting group title	OA 40/10
Reporting group description:	
Participants who received OA 40/10 along the entire active treatment period.	
Reporting group title	0lmesartan 20
Reporting group description:	
Participants who received O20 along the entire active treatment period.	
Reporting group title	Olmesartan 40
Reporting group description:	
Participants who received O40 along the entire active treatment period.	
Reporting group title	Amlodipine 5
Reporting group description:	
Participants who received A5 along the entire active treatment period.	
Reporting group title	Amlodipine 10
Reporting group description:	
Participants who received A10 along the entire active treatment period.	
Reporting group title	PLAC
Reporting group description:	
Participants who received placebo along the entire active treatment period.	

Serious adverse events	OA 20/5	OA 40/5	OA 40/10
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 129 (0.78%)	1 / 130 (0.77%)	0 / 129 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Syncope			

subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	0lmesartan 20	Olmesartan 40	Amlodipine 5
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Amlodipine 10	PLAC	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	OA 20/5	OA 40/5	OA 40/10
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 129 (16.28%)	24 / 130 (18.46%)	38 / 129 (29.46%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 129 (0.78%)	1 / 130 (0.77%)	3 / 129 (2.33%)
occurrences (all)	1	1	3
Hypotension			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	1	0	3
Hot flush			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	9 / 129 (6.98%)
occurrences (all)	1	0	10

Asthenia			
subjects affected / exposed	1 / 129 (0.78%)	3 / 130 (2.31%)	0 / 129 (0.00%)
occurrences (all)	1	3	0
Local swelling			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
No adverse event			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	2 / 129 (1.55%)
occurrences (all)	0	0	2
Chest discomfort			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	1 / 129 (0.78%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Sinobronchitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALT increased			
subjects affected / exposed	1 / 129 (0.78%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	1	1	0
Blood urea increased			
subjects affected / exposed	1 / 129 (0.78%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Arthroscopy			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
AST increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Blood pressure decreased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Crystal urine present			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Haematocrit decreased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Heart rate increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Red blood cell count decreased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Weight increased			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	2 / 129 (1.55%)
occurrences (all)	0	0	2
Arthropod bite			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 129 (1.55%)	2 / 130 (1.54%)	7 / 129 (5.43%)
occurrences (all)	2	2	7
Dizziness			
subjects affected / exposed	5 / 129 (3.88%)	3 / 130 (2.31%)	6 / 129 (4.65%)
occurrences (all)	5	3	6
Somnolence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Hypotonia			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	1 / 129 (0.78%)
occurrences (all)	0	1	1
Ear discomfort			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Vertigo positional			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Eye disorders			
Photopsia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Diarrhoea			

subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Anal haemorrhage			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Ileus paralytic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0
Skin irritation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Haemoglobinuria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Calculus ureteric			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Renal colic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	3 / 129 (2.33%)
occurrences (all)	0	0	4
Back pain			
subjects affected / exposed	0 / 129 (0.00%)	2 / 130 (1.54%)	0 / 129 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	2
Muscle spasms			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 130 (0.77%)	1 / 129 (0.78%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Acute tonsillitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 129 (0.00%)	2 / 130 (1.54%)	0 / 129 (0.00%)
occurrences (all)	0	2	0
Hyperglycaemia			
subjects affected / exposed	1 / 129 (0.78%)	1 / 130 (0.77%)	0 / 129 (0.00%)
occurrences (all)	1	1	0
Decreased appetite			
subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Diabetes mellitus			

subjects affected / exposed	0 / 129 (0.00%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 130 (0.00%)	0 / 129 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	0lmesartan 20	Olmesartan 40	Amlodipine 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 97 (23.71%)	21 / 96 (21.88%)	13 / 97 (13.40%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 97 (1.03%)	2 / 96 (2.08%)	1 / 97 (1.03%)
occurrences (all)	1	2	1
Hypotension			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 97 (0.00%)	4 / 96 (4.17%)	4 / 97 (4.12%)
occurrences (all)	0	4	4
Asthenia			
subjects affected / exposed	1 / 97 (1.03%)	2 / 96 (2.08%)	0 / 97 (0.00%)
occurrences (all)	1	2	0
Local swelling			
subjects affected / exposed	1 / 97 (1.03%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	1	1	0
No adverse event			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			

subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Sinobronchitis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Apathy			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Mood altered			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALT increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
White blood cell count increased			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Arthroscopy			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
AST increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0

Blood pressure decreased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Crystal urine present			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Arthropod bite			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 97 (2.06%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	2	0	1
Palpitations			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 97 (1.03%)	2 / 96 (2.08%)	2 / 97 (2.06%)
occurrences (all)	1	2	2
Dizziness			
subjects affected / exposed	1 / 97 (1.03%)	3 / 96 (3.13%)	1 / 97 (1.03%)
occurrences (all)	1	3	1
Somnolence			
subjects affected / exposed	0 / 97 (0.00%)	2 / 96 (2.08%)	0 / 97 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Hypotonia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 97 (0.00%)	2 / 96 (2.08%)	0 / 97 (0.00%)
occurrences (all)	0	2	0
Ear discomfort			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Photopsia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Toothache			

subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Anal haemorrhage			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Ileus paralytic			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haemoglobinuria			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Calculus ureteric			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Glycosuria			

subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Renal colic			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 97 (1.03%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			

subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	1 / 97 (1.03%)
occurrences (all)	0	0	1
Acute tonsillitis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 97 (0.00%)	1 / 96 (1.04%)	0 / 97 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 96 (0.00%)	0 / 97 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Amlodipine 10	PLAC	
Total subjects affected by non-serious adverse events			

subjects affected / exposed	32 / 98 (32.65%)	12 / 65 (18.46%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 98 (1.02%)	2 / 65 (3.08%)	
occurrences (all)	1	2	
Hypotension			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	12 / 98 (12.24%)	0 / 65 (0.00%)	
occurrences (all)	12	0	
Asthenia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Local swelling			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
No adverse event			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Chest discomfort			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	

Oedema			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Dysphonia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Sinobronchitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Apathy			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Mood altered			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Investigations			
ALT increased			

subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Arthroscopy			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
AST increased			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood pressure decreased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Crystal urine present			

subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Haematocrit decreased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Heart rate increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Arthropod bite			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Palpitations			

subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 98 (2.04%)	4 / 65 (6.15%)	
occurrences (all)	2	5	
Dizziness			
subjects affected / exposed	2 / 98 (2.04%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Somnolence			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hypotonia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Ear discomfort			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Tinnitus			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Vertigo positional			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Photopsia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 98 (2.04%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 98 (1.02%)	1 / 65 (1.54%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Anal haemorrhage			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Constipation			

subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Ileus paralytic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 98 (2.04%)	0 / 65 (0.00%)	
occurrences (all)	2	0	
Dermatitis allergic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Psoriasis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Skin irritation			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haemoglobinuria			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	1	
Calculus ureteric			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Glycosuria			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Proteinuria			

subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Renal colic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	4 / 98 (4.08%)	0 / 65 (0.00%)	
occurrences (all)	4	0	
Back pain			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 98 (2.04%)	1 / 65 (1.54%)	
occurrences (all)	2	1	
Gastroenteritis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Acute tonsillitis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 65 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 98 (0.00%)	1 / 65 (1.54%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Decreased appetite			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Diabetes mellitus			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 65 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2014	Amendment was requested by the competent German regulatory authority (BfArm) and included additional information/clarification on the contraception and pregnancy testing methology in accordance with "HMA/CTFG Recommendations related to contraception and pregnancy testing in clinical trials. Final version, 2014-09-15". Hence, Exclusion criteria were reformulated and additional pregnancy tests were included for female subjects of childbearing potential.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported