Clinical trial results:
Olmesartan + Amlodipine treatment in diabetic patients: evaluating blood pressure control after 48 hours from the last administration (missed dose).

Summary

EudraCT number	2010-018774-21
Trial protocol	ES FR DE GR IT
Global end of trial date	15 May 2014

Results information

Result version number	v1 (current)
This version publication date	26 February 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	MeIn/08/OLMAML-Hyp/001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Menarini International Operations Luxembourg S.A.
Sponsor organisation address	1, Avenue de la Gare, Luxembourg, Luxembourg, L-1611
Public contact	Medical Scientific Management, Menarini International Operations Luxembourg S.A., +352 264976,
Scientific contact	Menarini Corporate Medical Department, Menarini Industrie Farmaceutiche Riunite, +39 05556801,

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	15 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether the Olmesartan (OLM) 20-40 mg + Amlodipine (AML) 5-10 mg combination was at least as effective as the Perindopril (PER) 4-8 mg + Amlodipine 5-10 mg combination in reducing office diastolic blood pressure after 24 weeks of treatment, at 48 hours from last administration (missed dose).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines and local law requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2010
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	Germany: 14
Country: Number of subjects enrolled	Greece: 25
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Italy: 187
Worldwide total number of subjects	260
EEA total number of subjects	260

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)	187
From 65 to 84 years	73
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Total recruitment period (first patient in to last patient in): about 152 weeks (03/12/2010-31/10/2013).

Pre-assignment

Screening details:

The pre-assignment period was a run-in period, open-label, during which the eligible patients took one Amlodipine 5 mg tablet every day for 7 or 14 days (for 1 or 2 weeks), depending on previous subject's treatment(s).

Pre-assignment period milestones

Number of subjects started	335[1]
Number of subjects completed	260

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Inclusion or exclusion criteria not met: 62
Reason: Number of subjects	Adverse event, non-fatal: 4
Reason: Number of subjects	Consent withdrawn by subject: 8
Reason: Number of subjects	missing reason: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: All the 335 patients screened for the study entered a pre-randomization run-in period of 7-14 days with Amlodipine 5 mg once a day (pre-assignment period). Out of these 335 subjects, 260 were randomized to one of the two study treatments, hence entering in baseline period (=period 1) population.

Period 1

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

Blinding implementation details:

The "double-dummy" technique with matching placebo guaranteed the maintenance of the clinical study double-blind conditions.
No blinding was used during the run-in period, when all patients received amlodipine 5mg tablet once-a-day.

Arms

Are arms mutually exclusive?	Yes
Arm title	OLM/AML

Arm description:

Olmesartan 20 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 10 mg FDC coated tablets, once a day, by oral route
For the first 12 weeks of randomised double-blind treatment, patients randomized to OLM/AML received a combination of Olmesartan 20 mg + Amlodipine 5 mg once-daily.
In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Olmesartan 40 mg + Amlodipine 5 mg once-daily.
In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Olmesartan 40 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one capsule and one tablet) in a single blind for 1 day.

Arm type	Experimental
Investigational medicinal product name	Olmesartan + amlodipine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

For the first 12 weeks of randomised double-blind treatment, patients randomized to OLM/AML received a combination of Olmesartan 20 mg + Amlodipine 5 mg once-daily.
In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Olmesartan 40 mg + Amlodipine 5 mg once-daily.
In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Olmesartan 40 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one capsule and one tablet) in a single blind for 1 day.
All drugs were administered orally, in the morning, at breakfast time, with a glass of water.

Arm title	PER/AML

Arm description:

Perindopril /Amlodipine fixed dose capsule, once a day, by oral route
Perindopril 4mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 10 mg fixed dose capsule

For the first 12 weeks of randomised double-blind treatment, patients randomized to PER/AML received Perindopril 4 mg + Amlodipine 5 mg once-daily. In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Perindopril 8 mg + Amlodipine 5 mg once-daily. In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Perindopril 8 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one placebo capsule and one placebo tablet) in a single blind for 1 day

Arm type	Active comparator
Investigational medicinal product name	Perindopril and amlodipine fixed combination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

For the first 12 weeks of randomised double-blind treatment, patients randomized to PER/AML received Perindopril 4 mg + Amlodipine 5 mg once-daily. In patients not normalised by treatment after 12 weeks the dose of drug treatment was be up-titrated to Perindopril 8 mg +
Amlodipine 5 mg once-daily. In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Perindopril 8 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one placebo
capsule and one placebo tablet) in a single blind for 1 day. All drugs were administered orally, in the morning, at breakfast time, with a glass of water.

Number of subjects in period 1	OLM/AML	PER/AML
Started	128	132
FInal placebo dosing at Visit 6	111	110
Completed	111	110
Not completed	17	22
Consent withdrawn by subject	3	6
SBP or DBP out of allowed range	5	-

Adverse event, non-fatal	4	3
Poor compliance	2	4
Inclusion or exclusion criteria not met	3	3
Investigator decision	-	1
SBP or DBP out of the allowed ranges	-	5

Baseline characteristics

Reporting groups

Reporting group title	OLM/AML

Reporting group description:

Olmesartan 20 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 10 mg FDC coated tablets, once a day, by oral route
For the first 12 weeks of randomised double-blind treatment, patients randomized to OLM/AML received a combination of Olmesartan 20 mg + Amlodipine 5 mg once-daily.
In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Olmesartan 40 mg + Amlodipine 5 mg once-daily.
In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Olmesartan 40 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one capsule and one tablet) in a single blind for 1 day.

Reporting group title	PER/AML

Reporting group description:

Perindopril /Amlodipine fixed dose capsule, once a day, by oral route
Perindopril 4mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 10 mg fixed dose capsule

For the first 12 weeks of randomised double-blind treatment, patients randomized to PER/AML received Perindopril 4 mg + Amlodipine 5 mg once-daily. In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Perindopril 8 mg + Amlodipine 5 mg once-daily. In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Perindopril 8 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one placebo capsule and one placebo tablet) in a single blind for 1 day

Reporting group values	OLM/AML	PER/AML	Total
Number of subjects	128	132	260
Age categorical Units: Subjects			
Adults (18-64 years)	91	96	187
From 65-84 years	37	36	73
Age continuous Units: years			
arithmetic mean	58.91	59.18	
standard deviation	± 7.47	± 7.29	-
Gender categorical Units: Subjects			
Female	41	47	88
Male	87	85	172

Subject analysis sets

Subject analysis set title	OLM/AML - safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population set included all randomised patients who had taken at least one dose of study medication.

Subject analysis set title	PER/AML - safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population set included all randomised patients who had taken at least one dose of study medication.

Subject analysis set title	OLM/AML - FAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

"Full Analysis Set" (FAS): according to the "Intention-to-Treat" (ITT) principle, this set included all randomised patients who took at least one dose of the study medication and with a baseline and at least one post-baseline efficacy assessment of sitting ODBP.

Subject analysis set title	PER/AML - FAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

"Full Analysis Set" (FAS): according to the "Intention-to-Treat" (ITT) principle, this set included all randomised patients who took at least one dose of the study medication and with a baseline and at least one post-baseline efficacy assessment of sitting ODBP.

Reporting group values	OLM/AML - safety	PER/AML - safety	OLM/AML - FAS
Number of subjects	128	132	126
Age categorical Units: Subjects			
Adults (18-64 years)	91	96	91
From 65-84 years	37	36	35
Age continuous Units: years			
arithmetic mean	58.91	59.18	58.78
standard deviation	± 7.47	± 7.29	± 7.46
Gender categorical Units: Subjects			
Female	41	47	40
Male	87	85	86

Reporting group values	PER/AML - FAS		
Number of subjects	130		
Age categorical Units: Subjects			
Adults (18-64 years)	94		
From 65-84 years	36		
Age continuous Units: years			
arithmetic mean	59.26		
standard deviation	± 7.32		
Gender categorical Units: Subjects			
Female	47		
Male	83		

End points

End points reporting groups

Reporting group title	OLM/AML

Reporting group description:

Olmesartan 20 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 5 mg FDC coated tablets, once a day, by oral route
Olmesartan 40 mg + Amlodipine 10 mg FDC coated tablets, once a day, by oral route
For the first 12 weeks of randomised double-blind treatment, patients randomized to OLM/AML received a combination of Olmesartan 20 mg + Amlodipine 5 mg once-daily.
In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Olmesartan 40 mg + Amlodipine 5 mg once-daily.
In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Olmesartan 40 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one capsule and one tablet) in a single blind for 1 day.

Reporting group title	PER/AML

Reporting group description:

Perindopril /Amlodipine fixed dose capsule, once a day, by oral route
Perindopril 4mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 5 mg fixed dose capsule
Perindopril 8mg/Amlodipine 10 mg fixed dose capsule

For the first 12 weeks of randomised double-blind treatment, patients randomized to PER/AML received Perindopril 4 mg + Amlodipine 5 mg once-daily. In patients not normalised by treatment after 12 weeks the dose of drug treatment was up-titrated to Perindopril 8 mg + Amlodipine 5 mg once-daily. In patients not yet normalised after additional 6 weeks of treatment (week 18) the dose of drug treatment was further up-titrated to Perindopril 8 mg + Amlodipine 10 mg once-daily. At visit 6a patients received placebo treatment (one placebo capsule and one placebo tablet) in a single blind for 1 day

Subject analysis set title	OLM/AML - safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population set included all randomised patients who had taken at least one dose of study medication.

Subject analysis set title	PER/AML - safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population set included all randomised patients who had taken at least one dose of study medication.

Subject analysis set title	OLM/AML - FAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

“Full Analysis Set” (FAS): according to the “Intention-to-Treat” (ITT) principle, this set included all randomised patients who took at least one dose of the study medication and with a baseline and at least one post-baseline efficacy assessment of sitting ODBP.

Subject analysis set title	PER/AML - FAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

“Full Analysis Set” (FAS): according to the “Intention-to-Treat” (ITT) principle, this set included all randomised patients who took at least one dose of the study medication and with a baseline and at least one post-baseline efficacy assessment of sitting ODBP.

Primary: Change from baseline in office brachial sitting DBP

End point title	Change from baseline in office brachial sitting DBP

End point description:

The office DBP measurement was done at the brachial artery level, after 24 weeks of active treatment, when patients were in sitting position, at 48h from the last administration (missed dose).

End point type	Primary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-11.71 (± 9.25)	-10.5 (± 8.76)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.058
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.886
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.129
upper limit	2.902

Notes:

[1] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in sitting office SBP

End point title	Change from baseline in sitting office SBP

End point description:

The office SBP measurement was done after 24 weeks of active treatment, when patients were in sitting position, at 48h from the last administration (missed dose).

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-16.35 (± 15.3)	-12.32 (± 12.81)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.112
upper limit	6.369

Notes:

[2] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline of sitting office SBP

End point title	Change from baseline of sitting office SBP

End point description:

The office SBP measurement was done after 24 weeks of active treatment.

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-19.61 (± 14.72)	-15.8 (± 12.92)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.713
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.521
upper limit	5.947

Notes:

[3] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in sitting office DBP

End point title	Change from baseline in sitting office DBP

End point description:

The office DBP measurement was done after 24 weeks of active treatment.

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-14.15 (± 8.79)	-13.18 (± 8.81)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	= 0.058
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.695

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.316
upper limit	2.705

Notes:

[4] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in sitting office pulse pressure

End point title	Change from baseline in sitting office pulse pressure

End point description:

The pulse pressure measurement was done after 24 weeks of active treatment at 48h from the last administration (missed dose).

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-4.64 (± 11.53)	-1.82 (± 11.26)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	= 0.099
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.194
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.341
upper limit	4.729

Notes:

[5] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in sitting office pulse pressure

End point title	Change from baseline in sitting office pulse pressure

End point description:

The pulse pressure measurement was done after 24 weeks of active treatment at 48h from the last administration (missed dose).

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	130		
Units: mmHg				
arithmetic mean (standard deviation)	-5.46 (± 12.08)	-2.62 (± 11.44)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	PER/AML - FAS v OLM/AML - FAS
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	= 0.099
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.967
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.562
upper limit	4.496

Notes:

[6] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Percentage of subjects with office sitting BP < 130/80 mmHg

End point title	Percentage of subjects with office sitting BP < 130/80 mmHg

End point description:

Rate of normalized subjects with Office sitting blood pressure <130/80 at V6a vs. baseline

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	122	125		
Units: percent				
number (not applicable)	23.77	20		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5388
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0.0377
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0654
upper limit	0.1408

Secondary: Percentage of subjects with office sitting BP < 130/80 mmHg

End point title	Percentage of subjects with office sitting BP < 130/80 mmHg
End point description:	
Rate of normalized subjects with Office sitting blood pressure <130/80 at V6b vs. baseline.	
End point type	Secondary
End point timeframe:	
At Visit 6b (or alternatively at early withdrawal)	

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	125		
Units: percent				
number (not applicable)	7.5	10.4		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	PER/AML - FAS v OLM/AML - FAS

Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	= 0.5056
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	-0.029
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1003
upper limit	0.0423

Notes:

[7] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Percentage of subjects with a sitting office SBP reduction of at least 20 mmHg or a sitting office DBP reduction of at least 10 mmHg

End point title	Percentage of subjects with a sitting office SBP reduction of at least 20 mmHg or a sitting office DBP reduction of at least 10 mmHg

End point description:

Rate of responders subjects at V6a vs. baseline

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	122	125		
Units: percent				
number (not applicable)	79.51	72.8		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
P-value	= 0.2351
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0.0671

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0388
upper limit	0.173

Notes:

[8] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Percentage of subjects with a sitting office SBP reduction of at least 20 mmHg or a sitting office DBP reduction of at least 10 mmHg

End point title	Percentage of subjects with a sitting office SBP reduction of at least 20 mmHg or a sitting office DBP reduction of at least 10 mmHg

End point description:

Rate of responders subjects at V6b vs. baseline.

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	125		
Units: percent				
number (not applicable)	64.17	60		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	= 0.5134
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0.0417
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0797
upper limit	0.1631

Notes:

[9] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in (aortic) central SBP

End point title	Change from baseline in (aortic) central SBP

End point description:

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-19.96 (± 13.29)	-12.91 (± 14.17)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	PER/AML - FAS v OLM/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	= 0.007
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	6.591
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.452
upper limit	12.73

Notes:

[10] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in (aortic) central SBP

End point title	Change from baseline in (aortic) central SBP

End point description:

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-16.99 (± 13.84)	-8.31 (± 16.12)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	= 0.007
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	8.155
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.861
upper limit	14.45

Notes:

[11] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in (aortic) central DBP

End point title	Change from baseline in (aortic) central DBP

End point description:

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-13.32 (± 9.95)	-11.12 (± 8.33)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
P-value	= 0.076
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.292
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.705
upper limit	6.288

Notes:

[12] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in (aortic) central DBP

End point title	Change from baseline in (aortic) central DBP

End point description:

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-12.14 (± 8.32)	-7.06 (± 8.13)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	= 0.076
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.194

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.106
upper limit	8.282

Notes:

[13] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in central pulse pressure

End point title	Change from baseline in central pulse pressure

End point description:

Change in central pulse pressure after 24 weeks of treatment

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	38		
Units: mmHg				
arithmetic mean (standard deviation)	-6.73 (± 10.67)	-1.89 (± 10.01)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.242
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.353
upper limit	8.837

Notes:

[14] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in central pulse pressure

End point title	Change from baseline in central pulse pressure

End point description:	
Change in central pulse pressure at 48 hours from last administration (missed dose)	
End point type	Secondary
End point timeframe:	
At Visit 6b (or alternatively at early withdrawal)	

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	38		
Units: mmHg				
arithmetic mean (standard deviation)	-5.02 (± 10.53)	-1.37 (± 11.86)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.944
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.759
upper limit	8.646

Notes:

[15] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in P1 height	
End point title	Change from baseline in P1 height
End point description:	
Change in P1 height (outgoing pressure wave) after 24 weeks of treatment	
End point type	Secondary
End point timeframe:	
At Visit 6a (or alternatively at early withdrawal)	

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-3.73 (± 5.84)	-0.56 (± 5.9)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
P-value	= 0.125
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.554
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.331
upper limit	5.438

Notes:

[16] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in P1 height

End point title	Change from baseline in P1 height

End point description:

Change in P1 height (outgoing pressure wave) at 48 hours from last administration (missed dose)

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: mmHg				
arithmetic mean (standard deviation)	-2.71 (± 5.97)	-0.95 (± 8.06)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS

Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	= 0.125
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.766
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.187
upper limit	4.719

Notes:

[17] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in ΔP

End point title	Change from baseline in ΔP
End point description:	
Change in ΔP (augmentation) after 24 weeks of treatment	
End point type	Secondary
End point timeframe:	
At Visit 6a (or alternatively at early withdrawal)	

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	38		
Units: mmHg				
arithmetic mean (standard deviation)	-3.51 (± 6)	-1.29 (± 5.43)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.197
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.252
upper limit	4.646

Notes:

[18] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in ΔP

End point title	Change from baseline in ΔP

End point description:

Change in ΔP (augmentation) at 48 hours from last administration (missed dose)

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	38		
Units: mmHg				
arithmetic mean (standard deviation)	-2.78 (± 6.04)	-0.21 (± 5.24)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.776
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.263
upper limit	5.289

Notes:

[19] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in Augmentation Index

End point title	Change from baseline in Augmentation Index

End point description:

Change in Augmentation Index after 24 weeks of treatment

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: percent				
arithmetic mean (standard deviation)	-3.64 (± 7.57)	-1.16 (± 6.89)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.407
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.074
upper limit	5.888

Notes:

[20] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in Augmentation Index

End point title	Change from baseline in Augmentation Index

End point description:

Change in Augmentation Index at 48 hours from last administration (missed dose)

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: percent				
arithmetic mean (standard deviation)	-3.19 (± 8.61)	1.19 (± 6.76)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.179
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.587
upper limit	7.772

Notes:

[21] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in pulse pressure amplification

End point title	Change from baseline in pulse pressure amplification

End point description:

Change in pulse pressure amplification after 24 weeks of treatment

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: ratio				
arithmetic mean (standard deviation)	0.05 (± 0.09)	0.0091 (± 0.11)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
P-value	= 0.024
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02796

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0792
upper limit	0.0232

Notes:

[22] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in pulse pressure amplification

End point title	Change from baseline in pulse pressure amplification

End point description:

Change in pulse pressure amplification at 48 hours from last administration (missed dose)

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	41		
Units: ratio				
arithmetic mean (standard deviation)	0.04 (± 0.13)	-0.02 (± 0.12)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	= 0.024
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05236
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1052
upper limit	0.0005

Notes:

[23] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in PWV

End point title	Change from baseline in PWV

End point description:

Change in Pulse wave velocity after 24 weeks of treatment

End point type	Secondary

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	29		
Units: m/sec				
arithmetic mean (standard deviation)	-0.92 (± 1.04)	-0.48 (± 1)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
P-value	= 0.0815
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.7849
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.058
upper limit	1.512

Notes:

[24] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Secondary: Change from baseline in PWV

End point title	Change from baseline in PWV

End point description:

Change in Pulse wave velocity at 48 hours from last administration (missed dose)

End point type	Secondary

End point timeframe:

At Visit 6b (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	29		
Units: m/sec				
arithmetic mean (standard deviation)	-0.53 (± 1.46)	0.21 (± 1.86)		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	= 0.0815
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.9259
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.214
upper limit	1.638

Notes:

[25] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Other pre-specified: Percentage of normalized subjects with office sitting blood pressure <140/85 mmHg

End point title	Percentage of normalized subjects with office sitting blood pressure <140/85 mmHg

End point description:

Exploratory endpoint established before unblinding

End point type	Other pre-specified

End point timeframe:

At Visit 6a (or alternatively at early withdrawal)

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	122	125		
Units: percent				
number (not applicable)	50	44		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
P-value	= 0.3735
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0643
upper limit	0.1843

Notes:

[26] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Other pre-specified: Percentage of normalized subjects with office sitting blood pressure <140/85 mmHg

End point title	Percentage of normalized subjects with office sitting blood pressure <140/85 mmHg
End point description:	
Exploratory endpoint established before unblinding	
End point type	Other pre-specified
End point timeframe:	
At Visit 6b (or alternatively at early withdrawal)	

End point values	OLM/AML - FAS	PER/AML - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	125		
Units: percent				
number (not applicable)	33.33	29.6		

Statistical analyses

Statistical analysis title	OLM/AML vs PER/AML
Comparison groups	OLM/AML - FAS v PER/AML - FAS
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
P-value	= 0.5827
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0.0373

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0789
upper limit	0.1536

Notes:

[27] - The statistical analyses were aimed to assess the non-inferiority and safety of combination Olmesartan + Amlodipine in comparison with Perindopril + Amlodipine.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety measurements are recorded at each visit from Visit 2 to Visit 6b.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.4

Reporting groups

Reporting group title	OLM/AML - safety
Reporting group description: -	
Reporting group title	PER/AML - safety

Reporting group description: -

Serious adverse events	OLM/AML - safety	PER/AML - safety	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 128 (0.78%)	2 / 132 (1.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Prostate transurethral resection			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of kidney stone			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (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	OLM/AML - safety	PER/AML - safety	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 128 (24.22%)	37 / 132 (28.03%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Naevus cell naevus			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Thrombophlebitis of the leg			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Peripheral oedema			
subjects affected / exposed	8 / 128 (6.25%)	11 / 132 (8.33%)	
occurrences (all)	8	11	
Asthenia			
subjects affected / exposed	2 / 128 (1.56%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Fever			
subjects affected / exposed	0 / 128 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Microlithiasis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Chest pain non-specific			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 128 (1.56%)	4 / 132 (3.03%)	
occurrences (all)	2	4	
Dry cough			
subjects affected / exposed	0 / 128 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Itching throat			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Psychiatric disorders			
Emotional distress			
subjects affected / exposed	2 / 128 (1.56%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Anxiety disorder			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Transient Insomnia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Closed dislocation of finger			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Knee sprain			

subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Sprained ankle			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 128 (1.56%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Palpitations aggravated			
subjects affected / exposed	1 / 128 (0.78%)	2 / 132 (1.52%)	
occurrences (all)	1	6	
Atrial fibrillation			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 128 (3.13%)	1 / 132 (0.76%)	
occurrences (all)	5	2	
Headache			
subjects affected / exposed	3 / 128 (2.34%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Lumbosacral root pain			
subjects affected / exposed	1 / 128 (0.78%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Burning sensation in face			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Headache aggravated			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Paraesthesia hand			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Ventricular arrhythmia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Abnormal vision			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Dyspepsia aggravated			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Stomach pain			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Itch			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	

Renal and urinary disorders			
Nycturia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 128 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Acking joints			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Cramps of lower extremities			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Muscle cramps			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Pain knee			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Shoulder pain			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 128 (2.34%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Bronchitis acute			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Common cold			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Flu			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	

Pulpitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Respiratory infection			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 128 (0.78%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	0 / 128 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2011	Amendment 1 was implemented in order to: - clarify how to manage the inclusion of patients taking Beta-blockers; - clarify how to perform PWV; - modify the exclusion criterion based on creatinine values, adding correct values; - correct definition of responder patients; - notify the change of the responsible person for co-ordination of monitoring activities at CRO
29 June 2011	Amendment 2 was implemented in order to: - allow inclusion of patients already treated with a combination therapy; - withdraw patients with SBP/DBP lower than 120/70; - clarify that previous HbA1c assessment was not necessary and that it could be analysed at V1 to be available at V2 before randomization; - correct typing errors.
09 July 2012	Amendment 3 was implemented in order to: - modify study phase from III to IV, Olmesartan + Amlodipine at all different dosages used in the study being available on Italian market; - add 30 Italian sites in the study, after the closure of all other sites located in France, Germany, Greece, Switzerland and Spain, due to low recruitment rate; - better describe Perindopril treatment and placebo; - change formulation for Perindopril + Amlodipine and related placebo from encapsulated in DB capsules size AA for oral use to tablets; - better describe study drugs packaging and labelling; - remind placebo administration at V6a; - turn CBP into optional assessment at V2, V4, V5, V6a and V6b or withdrawal, maintaining centralized reading; - correct typing errors; - notify the change of the responsible person for co-ordination of monitoring activities at CRO

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.

No limitations or caveats are applicable to this summary.

Notes: