Clinical trial results:
Dose-ranging Study to Evaluate the Safety and Efficacy of Olmesartan Medoxomil in Children and Adolescents With Hypertension

Summary

EudraCT number	2015-003329-32
Trial protocol	Outside EU/EEA
Global end of trial date	15 September 2008

Results information

Result version number	v1 (current)
This version publication date	20 November 2018
First version publication date	25 November 2016

Trial information

Trial identification

Sponsor protocol code	CS0866-A-U301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00151775
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo Pharma Development
Sponsor organisation address	399 Thornall Street, Edison, New Jersey, United States, 08837
Public contact	Clinical Trial Information, Daiichi Sankyo Development Ltd, +44 1753482800, euregaffairs@dsd-eu.com
Scientific contact	Clinical Trial Information, Daiichi Sankyo Development Ltd, +44 1753482800, euregaffairs@dsd-eu.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 September 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy and safety of Olmesartan Medoxomil in subjects 6 to 16 years of age with high Blood Pressure or hypertension.

Protection of trial subjects:

Subjects safety was assessed throughout the study by monitoring of adverse events (AEs) and routine laboratory safety tests, vital signs, and physical examination findings.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 162
Country: Number of subjects enrolled	India: 37
Country: Number of subjects enrolled	Argentina: 34
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Colombia: 19
Country: Number of subjects enrolled	Costa Rica: 6
Country: Number of subjects enrolled	South Africa: 82
Country: Number of subjects enrolled	Kenya: 2
Country: Number of subjects enrolled	Uganda: 8
Country: Number of subjects enrolled	Zambia: 5
Worldwide total number of subjects	362
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	9
Children (2-11 years)	158
Adolescents (12-17 years)	195
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 362 patients between 1 and 16 years of age were recruited on a global basis between 27 April 2005 and 15 September 2008.

Period 1

Period 1 title	Period 1: Screening
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All Patients

Arm description:

Period 1 was a screening, wash-out period of approximately two weeks. All participants were included in the screening, wash-out period and during this period no intervention was administered.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	All Patients
Started	362
Completed	362

Period 2

Period 2 title	Period 2: Double-blind, Dose Response
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Cohort A: High Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a high dose of olmesartan medoxomil suspension (OM), depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a high dose of olmesartan medoxomil, 20 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort A: Low Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a low dose of olmesartan medoxomil, 2.5 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort B: High Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a high dose of olmesartan medoxomil, 20 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort B: Low Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental

Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a low dose of olmesartan medoxomil, 2.5 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort C: OM in Periods 2, 3, and 4

Arm description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received olmesartan medoxomil suspension (OM), 0.3 mg/kg orally once daily for 3 weeks.

Notes:

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

Justification: Period 1 is not the baseline period because it was a screening and wash-out period before randomization, so all subjects were included.

Number of subjects in period 2	Cohort A: High Dose OM in Periods 2 and 3	Cohort A: Low Dose OM in Periods 2 and 3	Cohort B: High Dose OM in Periods 2 and 3
Started	95	95	56
Completed	93	89	54
Not completed	2	6	2
Blood pressure goal was met	-	-	-
Physician decision	-	-	1
Adverse event, non-fatal	1	2	-
Unknown	-	-	-
Lost to follow-up	1	-	-
Protocol deviation	-	4	1

Number of subjects in period 2	Cohort B: Low Dose OM in Periods 2 and 3	Cohort C: OM in Periods 2, 3, and 4
Started	56	60
Completed	53	59
Not completed	3	1
Blood pressure goal was met	1	-
Physician decision	-	-
Adverse event, non-fatal	-	-

Unknown	1	-
Lost to follow-up	1	1
Protocol deviation	-	-

Period 3

Period 3 title	Period 3: Double-blind, Withdrawal
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: High Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a high dose of olmesartan medoxomil suspension (OM), depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a high dose of olmesartan medoxomil, 20 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort A: Low Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a low dose of olmesartan medoxomil, 2.5 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort B: High Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2

(double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a high dose of olmesartan medoxomil, 20 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort B: Low Dose OM in Periods 2 and 3

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received a low dose of olmesartan medoxomil, 2.5 mg orally once daily for patients weighing more than 20 kg and less than 35 kg, and 40 mg once daily for patients weighing 35 kg or more.

Arm title	Cohort C: OM in Periods 2, 3, and 4

Arm description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received olmesartan medoxomil suspension (OM), 0.3 mg/kg orally once daily for 3 weeks.

Arm title	Cohort A: Placebo in Period 3 (From High Dose in Period 2)

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black participants) given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous high dose of OM.

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

Dosage and administration details:

Patients received placebo orally once daily.

Arm title	Cohort A: Placebo in Period 3 (From Low Dose in Period 2)

Arm description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous low dose of OM.

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

Dosage and administration details:

Patients received placebo orally once daily.

Arm title	Cohort B: Placebo in Period 3 (From High Dose in Period 2)

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black patients), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous high dose of OM.

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

Dosage and administration details:

Patients received placebo orally once daily.

Arm title	Cohort B: Placebo in Period 3 (From Low Dose in Period 2)

Arm description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black patients), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous low dose of OM.

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

Dosage and administration details:

Patients received placebo orally once daily.

Arm title	Cohort C: Placebo in Period 3 (From OM in Period 2)

Arm description:

Patients in subgroup of Cohort C (1-5 years old), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5).

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients received placebo orally once daily.

Number of subjects in period 3[2]	Cohort A: High Dose OM in Periods 2 and 3	Cohort A: Low Dose OM in Periods 2 and 3	Cohort B: High Dose OM in Periods 2 and 3
Started	48	45	26
Completed	48	45	25
Not completed	0	0	1
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	-
Met blood pressure goal	-	-	-
Unknown	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 3[2]	Cohort B: Low Dose OM in Periods 2 and 3	Cohort C: OM in Periods 2, 3, and 4	Cohort A: Placebo in Period 3 (From High Dose in Period 2)
Started	27	29	45
Completed	26	29	42
Not completed	1	0	3
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	1
Met blood pressure goal	1	-	-
Unknown	-	-	1
Lost to follow-up	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 3[2]	Cohort A: Placebo in Period 3 (From Low Dose in Period 2)	Cohort B: Placebo in Period 3 (From High Dose in Period 2)	Cohort B: Placebo in Period 3 (From Low Dose in Period 2)
Started	44	28	26
Completed	44	27	26
Not completed	0	1	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Met blood pressure goal	-	-	-
Unknown	-	1	-
Lost to follow-up	-	-	-

Protocol deviation	-	-	-

Number of subjects in period 3[2]	Cohort C: Placebo in Period 3 (From OM in Period 2)
Started	29
Completed	28
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Met blood pressure goal	-
Unknown	-
Lost to follow-up	1
Protocol deviation	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: This trial has a crossover component and multiple sub-groups, so the number of participants in each group is not as expected.

Period 4

Period 4 title	Period 4:Open Label, Safety Analysis Set
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Period 4 Open-label Olmesartan

Arm description:

All remaining members of Cohort A (6-16 years old with a limit on the number of Black patients) were given 10 mg to 40 mg of olmesartan administered as oral suspension or tablets, depending on patient weight and response in the open-label Period 4 (weeks 6-51). Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 10 mg olmesartan medoxomil suspension or 20 mg tablet(s) orally once daily for 46 weeks.

Arm title	Cohort B: Period 4 Open-label Olmesartan

Arm description:

All remaining members of Cohort B (6-16 years old comprised exclusively of Black patients) were given 10 mg to 40 mg of olmesartan administered as oral suspension or tablets, depending on patient weight and response in the open-label Period 4 (weeks 6-51). Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Arm type	Experimental

Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 10 mg olmesartan medoxomil suspension or 20 mg tablet(s) orally once daily for 46 weeks.

Arm title	Cohort C: OM in Periods 2, 3, and 4

Arm description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C (who received OM in Periods 2 and 3) received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Number of subjects in period 4	Cohort A: Period 4 Open-label Olmesartan	Cohort B: Period 4 Open-label Olmesartan	Cohort C: OM in Periods 2, 3, and 4
Started	179	104	57
Completed	149	83	57
Not completed	30	21	0
Consent withdrawn by subject	5	2	-
Physician decision	-	2	-
Adverse event, non-fatal	1	2	-
Unknown	1	3	-
Increased blood pressure	1	1	-
Lost to follow-up	17	7	-
Non-compliance with Protocol	4	4	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: High Dose OM in Periods 2 and 3
Reporting group description:	
Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a high dose of olmesartan medoxomil suspension (OM), depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).	
Reporting group title	Cohort A: Low Dose OM in Periods 2 and 3
Reporting group description:	
Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).	
Reporting group title	Cohort B: High Dose OM in Periods 2 and 3
Reporting group description:	
Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).	
Reporting group title	Cohort B: Low Dose OM in Periods 2 and 3
Reporting group description:	
Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).	
Reporting group title	Cohort C: OM in Periods 2, 3, and 4
Reporting group description:	
Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.	

Reporting group values	Cohort A: High Dose OM in Periods 2 and 3	Cohort A: Low Dose OM in Periods 2 and 3	Cohort B: High Dose OM in Periods 2 and 3
Number of subjects	95	95	56
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous			
Units: years			
arithmetic mean	12.1	12.3	12.2
standard deviation	± 2.97	± 2.98	± 2.83
Gender categorical			
Units: Subjects			
Female	33	35	35
Male	62	60	21

Reporting group values	Cohort B: Low Dose OM in Periods 2 and 3	Cohort C: OM in Periods 2, 3, and 4	Total
Number of subjects	56	60	362
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	12.8	3.4	
standard deviation	± 2.42	± 1.45	-
Gender categorical			
Units: Subjects			
Female	20	26	149
Male	36	34	213

End points reporting groups

Reporting group title	All Patients

Reporting group description:

Period 1 was a screening, wash-out period of approximately two weeks. All participants were included in the screening, wash-out period and during this period no intervention was administered.

Reporting group title	Cohort A: High Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a high dose of olmesartan medoxomil suspension (OM), depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort A: Low Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort B: High Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort B: Low Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort C: OM in Periods 2, 3, and 4

Reporting group description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Reporting group title	Cohort A: High Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a high dose of olmesartan medoxomil suspension (OM), depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort A: Low Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort B: High Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort B: Low Dose OM in Periods 2 and 3

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black subjects) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period from day 0 to week 3). Half of the subjects continued this dose into Period 3 (double-blind, placebo controlled period from week 3 to week 5).

Reporting group title	Cohort C: OM in Periods 2, 3, and 4

Reporting group description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Reporting group title	Cohort A: Placebo in Period 3 (From High Dose in Period 2)

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black participants) given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous high dose of OM.

Reporting group title	Cohort A: Placebo in Period 3 (From Low Dose in Period 2)

Reporting group description:

Patients in subgroup of Cohort A (6-16 years old with a limit on the number of Black patients) given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous low dose of OM.

Reporting group title	Cohort B: Placebo in Period 3 (From High Dose in Period 2)

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black patients), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous high dose of OM.

Reporting group title	Cohort B: Placebo in Period 3 (From Low Dose in Period 2)

Reporting group description:

Patients in subgroup of Cohort B (6-16 years old comprised exclusively of Black patients), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5) instead of the previous low dose of OM.

Reporting group title	Cohort C: Placebo in Period 3 (From OM in Period 2)

Reporting group description:

Patients in subgroup of Cohort C (1-5 years old), given placebo during Period 3 (double-blind, placebo-controlled period from week 3 to week 5).

Reporting group title	Cohort A: Period 4 Open-label Olmesartan

Reporting group description:

All remaining members of Cohort A (6-16 years old with a limit on the number of Black patients) were given 10 mg to 40 mg of olmesartan administered as oral suspension or tablets, depending on patient weight and response in the open-label Period 4 (weeks 6-51). Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Reporting group title	Cohort B: Period 4 Open-label Olmesartan

Reporting group description:

All remaining members of Cohort B (6-16 years old comprised exclusively of Black patients) were given 10 mg to 40 mg of olmesartan administered as oral suspension or tablets, depending on patient weight and response in the open-label Period 4 (weeks 6-51). Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Reporting group title	Cohort C: OM in Periods 2, 3, and 4

Reporting group description:

Patients in subgroup of cohort C (1-5 years old) were given olmesartan medoxomil 0.3 mg/kg in Period 2 (open-label period from day 0 to week 3) and patients in a subgroup of Cohort C were given that dose of OM during Period 3 (double-blind, placebo controlled period from week 3 to week 5). In Period 4 (open-label period from weeks 6-51), all patients in Cohort C (who received OM in Periods 2 and 3) received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks, the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin

receptor blocker) were allowed if hypertension was not controlled.

Subject analysis set title	Cohort A: High Dose OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup of Cohort A (6-16 years old with a limit on the number of Black participants) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period).

Subject analysis set title	Cohort A: Low Dose OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup of Cohort A (6-16 years old with a limit on the number of Black participants) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period).

Subject analysis set title	Cohort B: High Dose OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup of Cohort B (6-16 years old comprised exclusively of Black participants) given a high dose (20 mg or 40 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period).

Subject analysis set title	Cohort B: Low Dose OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup of Cohort B (6-16 years old comprised exclusively of Black participants) given a low dose (2.5 mg or 5.0 mg) of olmesartan medoxomil suspension (OM) depending on weight during Period 2 (double-blind, dose-response period). Half of the participants continued this dose into Period 3 (double-blind, placebo controlled period).

Subject analysis set title	Cohort C: OM (Olmesartan Medoxomil)
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort C (1-5 years old) was given olmesartan medoxomil (OM) 0.3 mg/kg in Period 2 (open-label period) and a subgroup of Cohort C was given that dose of OM during Period 3 (double-blind, placebo-controlled period). In Period 4 (open-label period), all of Cohort C received an OM starting dose of 0.3 mg/kg. If hypertension was not controlled after two week the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Subject analysis set title	Cohort A
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort A participants were 6-16 years old with a limit on the number of Black participants. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (20 mg or 40 mg) and the low dose (2.5 mg or 5.0mg), depending on weight, administered once daily.

Subject analysis set title	Cohort B
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort B participants were 6-16 years old and comprised exclusively of Black participants. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (20 mg or 40 mg) and the low dose (2.5 mg or 5.0 mg), depending on weight, administered once daily.

Subject analysis set title	Cohorts A + B
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort A + B participants were 6-16 years old. Cohort A limited the number of Black participants, while Cohort B was comprised exclusively of Black participants. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (20 mg or 40 mg) and the low dose (2.5 mg or 5.0mg), depending on weight, administered once daily.

Subject analysis set title	Cohorts A + B: Low Dose OM

Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup from Cohorts A + B (6-16 years old) who received the low dose of olmesartan medoxomil suspension (OM 2.5 mg or 5.0 mg depending on weight), administered once daily in Period 2. Cohort A limited the number of Black participants, while Cohort B was comprised exclusively of Black participants.

Subject analysis set title	Cohorts A + B: High Dose OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subgroup from Cohorts A + B (6-16 years old) who received the high dose of olmesartan medoxomil suspension (OM 20 mg or 40 mg depending on weight), administered once daily in Period 2. Cohort A limited the number of Black participants, while Cohort B was comprised exclusively of Black participants.

Subject analysis set title	Cohort A: OM Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort A participants were 6-16 years old with a limit on the number of Black participants. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (OM 20 mg or 40 mg) and the low dose (2.5 mg or 5.0mg), depending on weight, administered once daily in period 2, and continued that dosage into period 3.

Subject analysis set title	Cohort A: Placebo Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort A participants were 6-16 years old with a limit on the number of Black participants. Includes participants randomized to both the high and low dose of olmesartan medoxomil suspension in period 2, and changed to placebo in period 3.

Subject analysis set title	Cohort B: OM Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort B participants were 6-16 years old and comprised exclusively of Black participants. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (OM 20 mg or 40 mg) and the low dose (2.5 mg or 5.0mg), depending on weight, administered once daily in period 2, and continued that dosage into period 3.

Subject analysis set title	Cohort B: Placebo Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort B participants were 6-16 years old and comprised exclusively of Black participants. Includes participants randomized to both the high and low dose of olmesartan medoxomil suspension in period 2, and changed to placebo in period 3.

Subject analysis set title	Cohorts A + B: OM Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort A + B participants were 6-16 years old. Includes participants randomized to both the high dose of olmesartan medoxomil suspension (OM 20 mg or 40 mg) and the low dose (2.5 mg or 5.0mg), depending on weight, administered once daily in period 2, and continued that dosage into period 3.

Subject analysis set title	Cohorts A + B: Placebo Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohorts A + B participants were 6-16 years old. Includes participants randomized to both the high and low dose of olmesartan medoxomil suspension in period 2, and changed to placebo in period 3.

Subject analysis set title	Cohort C: OM Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort C consisted of children from 1 to 5 years of age. There were no racial restrictions. This group continued on its Period 2 olmesartan dose of 0.3 mg/kg.

Subject analysis set title	Cohort C: Placebo Period 3
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort C consisted of children from 1 to 5 years of age. There were no racial restrictions. This group was

switched from its Period 2 olmesartan dose of 0.3 mg/kg to placebo.

Subject analysis set title	Cohorts A + B: Period 4 Open-label OM
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects of Cohorts A + B (6-16 years old) were given 10 mg to 40 mg of olmesartan (OM) administered as oral suspension or tablets depending on participant weight and response in the openlabel Period 4. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Primary: Least Squares Mean Change from Baseline in Seated Systolic Blood Pressure to the End of Period 2 (3 weeks)

End point title	Least Squares Mean Change from Baseline in Seated Systolic Blood Pressure to the End of Period 2 (3 weeks)

End point description:

The efficacy dose response change in trough seated systolic blood pressure (both non-weight adjusted and weight adjusted results) from baseline to the end of the dose-ranging period (Period 2). Non-weight adjusted dose was the fixed olmesartan medoxomil dose; weight adjusted dose calculated mg of olmesartan medoxomil per kg of weight at baseline. The number of participants includes all randomized to Cohort A, Cohort B and a combination of the two cohorts. The Last Observation Carried Forward method was used in the linear regression analysis for the change in the seated systolic blood pressure from baseline to the end of three weeks.

End point type	Primary

End point timeframe:

Day 0 to 3 weeks

End point values	Cohort A	Cohort B	Cohorts A + B	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	190	112	302	
Units: millimeter of mercury (mm Hg)				
least squares mean (standard error)				
Non-weight adjusted dosage	-0.69 (± 0.202)	-0.85 (± 0.282)	-0.75 (± 0.165)	
Weight adjusted dosage	-8.97 (± 2.054)	-7.17 (± 3.19)	-8.36 (± 1.75)	

Statistical analyses

Statistical analysis title	Cohort A Non-weight adjusted dosage
Comparison groups	Cohort A v Cohort B v Cohorts A + B
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008
Method	Regression, Linear

Statistical analysis title	Cohort A Weight adjusted dosage
Comparison groups	Cohort A v Cohort B v Cohorts A + B

Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Cohort B Non-weight adjusted dosage
Comparison groups	Cohort B v Cohort A v Cohorts A + B
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0032
Method	Regression, Linear

Statistical analysis title	Cohort B Weight adjusted dosage
Comparison groups	Cohort B v Cohort A v Cohorts A + B
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Linear

Statistical analysis title	Cohorts A + B Weight adjusted dosage
Comparison groups	Cohorts A + B v Cohort A v Cohort B
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Cohorts A + B Non-weight adjusted dosage
Comparison groups	Cohorts A + B v Cohort A v Cohort B
Number of subjects included in analysis	604
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Regression, Linear

Primary: Mean Change from Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 2 (3 weeks)

End point title	Mean Change from Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 2 (3 weeks)

End point description:

Mean change from baseline to the end of the dose ranging period in systolic and diastolic blood pressure readings for Cohort A, Cohort B and Cohorts A+B combined. The Intent-to-Treat (ITT) population for Period II of the study was defined as subjects who took at least one dose of study medication and had study baseline and at least one seated systolic, or diastolic blood pressure measurement after taking study medication. The Last Observation carried forward was used.

End point type	Primary

End point timeframe:

Day 0 (baseline) to 3 weeks

End point values	Cohort A: High Dose OM	Cohort A: Low Dose OM	Cohort B: High Dose OM	Cohort B: Low Dose OM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	94	94	56	56
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	-12.58 (± 10.157)	-7.76 (± 9.18)	-10.68 (± 9.259)	-4.73 (± 11.483)
Change in Diastolic Blood Pressure	-9.5 (± 9.757)	-5.52 (± 8.058)	-7.58 (± 8.172)	-3.49 (± 8.844)

End point values	Cohorts A + B: Low Dose OM	Cohorts A + B: High Dose OM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	150	150		
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	-6.63 (± 10.17)	-11.87 (± 9.843)		
Change in Diastolic Blood Pressure	-4.76 (± 8.389)	-8.78 (± 9.216)		

Statistical analyses

Statistical analysis title	Statistical Analysis_1

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort A: High Dose OM v Cohort A: Low Dose OM

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0008
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_2

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort A: Low Dose OM v Cohort A: High Dose OM
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0026
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_3

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort B: Low Dose OM v Cohort B: High Dose OM
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0032
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_5

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohorts A + B: Low Dose OM v Cohorts A + B: High Dose OM
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_4

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in

seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort B: Low Dose OM v Cohort B: High Dose OM
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0125
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_6

Statistical analysis description:

A linear regression analysis of olmesartan dose (non-weight adjusted) on the change from baseline in seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohorts A + B: Low Dose OM v Cohorts A + B: High Dose OM
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_7

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort A: Low Dose OM v Cohort A: High Dose OM
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_8

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort A: Low Dose OM v Cohort A: High Dose OM
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_9

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort B: Low Dose OM v Cohort B: High Dose OM
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0265
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_10

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohort B: Low Dose OM v Cohort B: High Dose OM
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0084
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_11

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated systolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohorts A + B: Low Dose OM v Cohorts A + B: High Dose OM
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear

Statistical analysis title	Statistical Analysis_12

Statistical analysis description:

A linear regression analysis of olmesartan dose (weight adjusted) on the change from baseline in seated diastolic blood pressure was carried out. The null hypothesis of zero-slope was tested.

Comparison groups	Cohorts A + B: Low Dose OM v Cohorts A + B: High Dose OM
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Slope

Secondary: Mean Change From Period 3 Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 3

End point title	Mean Change From Period 3 Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 3

End point description:

Mean change from period 3 baseline (completion of the dose adjustment period and prior to starting the treatment of period 3) to the end of period 3 (double-blind placebo-controlled period) in seated systolic and diastolic blood pressure readings for Cohort A, Cohort B, Cohorts A+B combined and Cohort C. Intent to treat population defined as subjects who finished Period 2, had the end of Period 2 seated systolic or diastolic blood pressure measurement, took the Period 3 study medication for at least one week, and had the end of Period 3 seated systolic or diastolic blood pressure measurement. Intent-to-treat population defined as subjects who finished Period 2, had the end of Period 2 seated systolic or diastolic blood pressure measurement, took the Period 3 study medication for at least one week, and had the end of Period 3 seated systolic or diastolic blood pressure measurement.

End point type	Secondary

End point timeframe:

Week 3 (period 3 baseline) to week 5 (end of Period 3)

End point values	Cohort A: OM Period 3	Cohort A: Placebo Period 3	Cohort B: OM Period 3	Cohort B: Placebo Period 3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	93	89	53	54
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	0.43 (± 9.46)	4.93 (± 9.62)	1.37 (± 9.5)	3.79 (± 10)
Change in Diastolic Blood Pressure	0.24 (± 8.12)	4.43 (± 10.15)	1.94 (± 7.1)	3.25 (± 8.74)

End point values	Cohorts A + B: OM Period 3	Cohorts A + B: Placebo Period 3	Cohort C: OM Period 3	Cohort C: Placebo Period 3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	146	143	29	29
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	0.77 (± 9.451)	4.5 (± 9.745)	1.36 (± 8.994)	4.95 (± 8.568)
Change in Diastolic Blood Pressure	0.85 (± 7.79)	3.99 (± 9.627)	0.31 (± 8.556)	3.77 (± 7.203)

Statistical analyses

Statistical analysis title	Statistical Analysis_1

Statistical analysis description:

Analysis of systolic blood pressure. Null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 93 for Cohort A: OM Period 3 and 89 for Cohort A: Placebo Period 3.

Comparison groups	Cohort A: OM Period 3 v Cohort A: Placebo Period 3
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0093
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.27
upper limit	-0.89

Statistical analysis title	Statistical Analysis_2

Statistical analysis description:

Analysis for diastolic blood pressure. The null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 93 for Cohort A: OM Period 3 and 89 for Cohort A: Placebo Period 3.

Comparison groups	Cohort A: OM Period 3 v Cohort A: Placebo Period 3
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0052
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-3.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	-1.05

Statistical analysis title	Statistical Analysis_3

Statistical analysis description:

Analysis of systolic blood pressure. Null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 53 for Cohort B: OM Period 3 and 54 for Cohort B: Placebo Period 3.

Comparison groups	Cohort B: OM Period 3 v Cohort B: Placebo Period 3
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.93
upper limit	0.79

Statistical analysis title	Statistical Analysis_4

Statistical analysis description:

Analysis for diastolic blood pressure. The null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 53 for Cohort B: OM Period 3 and 54 for Cohort B: Placebo Period 3.

Comparison groups	Cohort B: OM Period 3 v Cohort B: Placebo Period 3
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3442
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.27
upper limit	1.5

Statistical analysis title	Statistical Analysis_5

Statistical analysis description:

For seated systolic blood pressure the null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 146 for Cohorts A + B: OM Period 3 and 143 for Cohorts A + B: Placebo Period 3.

Comparison groups	Cohorts A + B: OM Period 3 v Cohorts A + B: Placebo Period 3
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0029
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.24
upper limit	-1.09

Statistical analysis title	Statistical Analysis_6

Statistical analysis description:

For seated diastolic blood pressure the null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 146 for Cohorts A + B: OM Period 3 and 143 for Cohorts A + B: Placebo Period 3.

Comparison groups	Cohorts A + B: OM Period 3 v Cohorts A + B: Placebo Period 3
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0032
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.65
upper limit	-0.95

Statistical analysis title	Statistical Analysis_7

Statistical analysis description:

For seated systolic blood pressure the null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 29 for Cohort C: OM Period 3 and 29 for Cohort C: Placebo Period 3.

Comparison groups	Cohort C: OM Period 3 v Cohort C: Placebo Period 3
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2113
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.29
upper limit	1.65

Statistical analysis title	Statistical Analysis_8

Statistical analysis description:

For seated diastolic blood pressure the null hypothesis of no treatment difference was tested. The number of subjects included in analysis was 29 for Cohort C: OM Period 3 and 29 for Cohort C: Placebo Period 3.

Comparison groups	Cohort C: OM Period 3 v Cohort C: Placebo Period 3

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1496
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	-2.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.92
upper limit	1.09

Secondary: Mean Change From Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 4 (end of study)

End point title	Mean Change From Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 4 (end of study)

End point description:

Mean change from baseline to the end of the open label Period 4 in seated systolic and diastolic blood pressure readings for Cohort A, Cohort B and Cohorts A+B combined. Intent to treat population includes participants with at least one visit in Period 4.

End point type	Secondary

End point timeframe:

Day 0 to week 51 (end of study)

End point values	Cohorts A + B: Period 4 Open-label OM			
Subject group type	Subject analysis set			
Number of subjects analysed	281			
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	-9.7 (± 11.01)			
Change in Diastolic Blood Pressure	-6.6 (± 9.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 4 (End of Study) for Cohort C

End point title	Mean Change From Baseline in Seated Systolic and Diastolic Blood Pressure Measurements to the End of Period 4 (End of Study) for Cohort C

End point description:

Mean change from baseline to the end of the open label Period 4 in seated systolic and diastolic blood pressure readings for Cohort C. Subjects included who received medication in Period 4.

End point type	Secondary

End point timeframe:

Day 0 to week 51 week (end of study)

End point values	Cohort C: OM (Olmesartan Medoxomil)			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: mm Hg				
arithmetic mean (standard deviation)				
Change in Systolic Blood Pressure	-15.7 (± 9.83)			
Change in Diastolic Blood Pressure	-13.3 (± 11.18)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected starting with the signing of the informed consent form and continuing through the end of the study (51 weeks).

Adverse event reporting additional description:

AEs observed by the investigator, or reported by the subject, and any remedial action taken, were recorded in the case report form by the investigator. The nature of each event, time of onset after drug administration, duration, and intensity were documented together with the investigator's opinion of the causal relationship to the treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	8.1

Reporting groups

Reporting group title	Cohort A: Period 2 Low Dose OM

Reporting group description:

For Cohort A (patients 6-16 years old) olmesartan medoxomil suspension (OM) providing 2.5 mg or 5 mg, depending on weight

Reporting group title	Cohort A: Period 2 High Dose OM

Reporting group description:

For Cohort A (patients 6-16 years old), olmesartan medoxomil suspension (OM) providing 20 mg or 40 mg, depending on weight

Reporting group title	Cohort A: Period 3 OM High Dose Continued

Reporting group description:

The 20 mg or 40 mg dose of olmesartan medoxomil suspension (OM) from the previous period was continued.

Reporting group title	Cohort A: Period 3 Placebo From High Dose

Reporting group description:

Placebo was given instead of the previous high dose of olmesartan.

Reporting group title	Cohort A: Period 3 OM Low Dose Continued

Reporting group description:

The 2.5 mg or 5 mg dose of olmesartan medoxomil suspension (OM) from the previous period was continued.

Reporting group title	Cohort A: Period 3 Placebo From Low Dose

Reporting group description:

Placebo was given instead of the previous low dose of olmesartan.

Reporting group title	Cohort A: Period 4 Open-label OM

Reporting group description:

10 mg to 40 mg of olmesartan was administered as oral suspension or tablets depending on patient weight and response. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.

Reporting group title	Cohort B: Period 2 High Dose OM

Reporting group description:

For Cohort B (participants 6-16 years old), olmesartan medoxomil suspension (OM) providing 20 mg or 40 mg, depending on weight.

Reporting group title	Cohort B: Period 2 Low Dose OM

Reporting group description:

For Cohort B (participants 6-16 years old), olmesartan medoxomil suspension (OM) providing 2.5 mg or 5 mg, depending on weight.

Reporting group title	Cohort B: Period 3 Placebo From High Dose

Reporting group description:

Placebo was given instead of the previous high dose of olmesartan.

Reporting group title	Cohort B: Period 3 OM Low Dose Continued
Reporting group description:	
The 2.5 mg or 5 mg dose of olmesartan medoxomil suspension (OM) from the previous period was continued.	
Reporting group title	Cohort B: Period 3 OM High Dose Continued
Reporting group description:	
The 20 mg or 40 mg dose of olmesartan medoximil suspension (OM) from the previous period was continued.	
Reporting group title	Cohort C: Period 3 Placebo From OM in Period 2
Reporting group description:	
The 0.3 mg/kg dose of olmesartan medoxomil suspension (OM) was discontinued for these participants. They were switched to placebo.	
Reporting group title	Cohort B: Period 3 Placebo From Low Dose
Reporting group description:	
Placebo was given instead of the previous low dose of olmesartan.	
Reporting group title	Cohort B: Period 4 Open-label OM
Reporting group description:	
10 mg to 40 mg of olmesartan was administered as oral suspension or tablets depending on patient weight and response. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.	
Reporting group title	Cohort C: Period 2 Open-label OM
Reporting group description:	
The dose of olmesarten medoxomil suspension (OM) was 0.3 mg/kg for all patients who were 1 to 5 years of age.	
Reporting group title	Cohort C: Period 3 OM Dose Continued
Reporting group description:	
The 0.3 mg/kg dose of OM was continued for these patients.	
Reporting group title	Cohort C: Period 4 Open-label OM
Reporting group description:	
Patients received an olmesartan medoxomil suspension (OM) starting dose of 0.3 mg/kg. If hypertension was not controlled after two weeks the dose was doubled. Additional antihypertensive drugs (not an angiotensin converting enzyme or angiotensin receptor blocker) were allowed if hypertension was not controlled.	

Serious adverse events	Cohort A: Period 2 Low Dose OM	Cohort A: Period 2 High Dose OM	Cohort A: Period 3 OM High Dose Continued
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 95 (1.05%)	2 / 95 (2.11%)	0 / 48 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			

subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Eye disorders			
Eye hemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Ophthalmoplegia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Vomiting			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Epistaxis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 95 (0.00%)	1 / 95 (1.05%)	0 / 48 (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
Mental disorder			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Suicide attempt			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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			
Ureteric stenosis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Infections and infestations			
Abcess limb			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Bronchitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Broncopneumonia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Pneumonia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Pyelonephritis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Sinusitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Upper respiratory infection			

subjects affected / exposed	0 / 95 (0.00%)	1 / 95 (1.05%)	0 / 48 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 95 (0.00%)	0 / 48 (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
Hypoproteinemia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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
Metabolic disorder			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (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	Cohort A: Period 3 Placebo From High Dose	Cohort A: Period 3 OM Low Dose Continued	Cohort A: Period 3 Placebo From Low Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events		0	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
General disorders and administration site conditions			
Anasarca			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Eye disorders			
Eye hemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Ophthalmoplegia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Epistaxis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Mental disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Suicide attempt			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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			
Ureteric stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Systemic lupus erythematosus			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Infections and infestations			
Abcess limb			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Broncopneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Pyelonephritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Sinusitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Upper respiratory infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Metabolism and nutrition disorders			

Diabetic ketoacidosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Hypoproteinemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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
Metabolic disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (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	Cohort A: Period 4 Open-label OM	Cohort B: Period 2 High Dose OM	Cohort B: Period 2 Low Dose OM
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 179 (11.17%)	0 / 56 (0.00%)	0 / 56 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		0
Investigations			
Laparoscopy			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Eye disorders			

Eye hemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Ophthalmoplegia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Vomiting			
subjects affected / exposed	2 / 179 (1.12%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Epistaxis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Mental disorder			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Suicide attempt			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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 and urinary disorders			
Ureteric stenosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 179 (1.12%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Infections and infestations			
Abcess limb			

subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Bronchitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Broncopneumonia			
subjects affected / exposed	3 / 179 (1.68%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Pyelonephritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Sinusitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (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
Hypoproteinemia			

subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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
Metabolic disorder			
subjects affected / exposed	1 / 179 (0.56%)	0 / 56 (0.00%)	0 / 56 (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	Cohort B: Period 3 Placebo From High Dose	Cohort B: Period 3 OM Low Dose Continued	Cohort B: Period 3 OM High Dose Continued
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 26 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Eye disorders			
Eye hemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Ophthalmoplegia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Mental disorder			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Suicide attempt			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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			
Ureteric stenosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Infections and infestations			
Abcess limb			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Bronchitis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Broncopneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Upper respiratory infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Hypoproteinemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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
Metabolic disorder			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (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	Cohort C: Period 3 Placebo From OM in Period 2	Cohort B: Period 3 Placebo From Low Dose	Cohort B: Period 4 Open-label OM
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	7 / 104 (6.73%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Eye disorders			
Eye hemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Ophthalmoplegia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			

Ovarian cyst			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Mental disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Suicide attempt			

subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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			
Ureteric stenosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abcess limb			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Broncopneumonia			

subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Pyelonephritis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Upper respiratory infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Hypoproteinemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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
Metabolic disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (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	Cohort C: Period 2	Cohort C: Period 3	Cohort C: Period 4

	Open-label OM	OM Dose Continued	Open-label OM
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	6 / 57 (10.53%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Laparoscopy			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Congenital, familial and genetic disorders			
Coarctation of the aorta			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Eye disorders			
Eye hemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmoplegia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Peritonitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Epistaxis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Mental disorder			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Suicide attempt			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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			
Ureteric stenosis			

subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Nephrotic syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Infections and infestations			
Abcess limb			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Bronchitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Broncopneumonia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Sinusitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Upper respiratory infection			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Hypoproteinemia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (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
Metabolic disorder			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Cohort A: Period 2 Low Dose OM	Cohort A: Period 2 High Dose OM	Cohort A: Period 3 OM High Dose Continued
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 95 (48.42%)	47 / 95 (49.47%)	15 / 48 (31.25%)
Investigations			
Blood urea increased			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 95 (2.11%)	9 / 95 (9.47%)	0 / 48 (0.00%)
occurrences (all)	2	11	0
Headache			
subjects affected / exposed	7 / 95 (7.37%)	14 / 95 (14.74%)	4 / 48 (8.33%)
occurrences (all)	11	24	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 95 (4.21%)	4 / 95 (4.21%)	3 / 48 (6.25%)
occurrences (all)	4	4	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	5 / 95 (5.26%)	3 / 95 (3.16%)	0 / 48 (0.00%)
occurrences (all)	7	3	0
Vomiting			
subjects affected / exposed	3 / 95 (3.16%)	1 / 95 (1.05%)	3 / 48 (6.25%)
occurrences (all)	3	1	3
Diarrhea			
subjects affected / exposed	2 / 95 (2.11%)	1 / 95 (1.05%)	0 / 48 (0.00%)
occurrences (all)	2	1	0
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	6 / 95 (6.32%)	1 / 95 (1.05%)	2 / 48 (4.17%)
occurrences (all)	7	1	2
Cough			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	3
Rhinorrhea			

subjects affected / exposed	3 / 95 (3.16%)	2 / 95 (2.11%)	0 / 48 (0.00%)
occurrences (all)	3	2	0
Epistaxis			
subjects affected / exposed	2 / 95 (2.11%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Proteinurea			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 95 (4.21%)	1 / 95 (1.05%)	0 / 48 (0.00%)
occurrences (all)	4	1	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 95 (4.21%)	7 / 95 (7.37%)	0 / 48 (0.00%)
occurrences (all)	4	7	0
Influenza			
subjects affected / exposed	0 / 95 (0.00%)	1 / 95 (1.05%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	2 / 95 (2.11%)	4 / 95 (4.21%)	0 / 48 (0.00%)
occurrences (all)	2	4	0
Otitis media acute			

subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Tonsilitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	2 / 95 (2.11%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 95 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort A: Period 3 Placebo From High Dose	Cohort A: Period 3 OM Low Dose Continued	Cohort A: Period 3 Placebo From Low Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 45 (13.33%)	9 / 45 (20.00%)	6 / 44 (13.64%)
Investigations			
Blood urea increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	2 / 44 (4.55%)
occurrences (all)	1	3	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Diarrhea			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Rhinorrhea			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	0 / 44 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Proteinurea			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Pharyngitis			
subjects affected / exposed	3 / 45 (6.67%)	2 / 45 (4.44%)	0 / 44 (0.00%)
occurrences (all)	3	2	0
Otitis media acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Tonsilitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 44 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort A: Period 4 Open-label OM	Cohort B: Period 2 High Dose OM	Cohort B: Period 2 Low Dose OM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 179 (71.51%)	9 / 56 (16.07%)	12 / 56 (21.43%)
Investigations			

Blood urea increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 179 (5.59%)	1 / 56 (1.79%)	0 / 56 (0.00%)
occurrences (all)	13	1	0
Headache			
subjects affected / exposed	30 / 179 (16.76%)	5 / 56 (8.93%)	3 / 56 (5.36%)
occurrences (all)	42	5	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	16 / 179 (8.94%)	1 / 56 (1.79%)	0 / 56 (0.00%)
occurrences (all)	21	1	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	10 / 179 (5.59%)	1 / 56 (1.79%)	0 / 56 (0.00%)
occurrences (all)	10	1	0
Vomiting			
subjects affected / exposed	11 / 179 (6.15%)	0 / 56 (0.00%)	1 / 56 (1.79%)
occurrences (all)	17	0	1
Diarrhea			
subjects affected / exposed	2 / 179 (1.12%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	12 / 179 (6.70%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	20	0	0
Cough			
subjects affected / exposed	24 / 179 (13.41%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	28	0	0
Rhinorrhea			
subjects affected / exposed	4 / 179 (2.23%)	0 / 56 (0.00%)	1 / 56 (1.79%)
occurrences (all)	4	0	1
Epistaxis			

subjects affected / exposed	3 / 179 (1.68%)	0 / 56 (0.00%)	1 / 56 (1.79%)
occurrences (all)	9	0	1
Nasal congestion			
subjects affected / exposed	9 / 179 (5.03%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	10	0	0
Asthma			
subjects affected / exposed	6 / 179 (3.35%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	11	0	0
Rhinitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Proteinurea			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	16 / 179 (8.94%)	1 / 56 (1.79%)	2 / 56 (3.57%)
occurrences (all)	17	1	2
Upper respiratory tract infection			
subjects affected / exposed	20 / 179 (11.17%)	0 / 56 (0.00%)	2 / 56 (3.57%)
occurrences (all)	25	0	2
Influenza			
subjects affected / exposed	10 / 179 (5.59%)	0 / 56 (0.00%)	2 / 56 (3.57%)
occurrences (all)	12	0	2
Pharyngitis			
subjects affected / exposed	7 / 179 (3.91%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	7	0	0
Otitis media acute			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Tonsilitis			

subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	4 / 179 (2.23%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	5	0	0
Viral infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 56 (0.00%)	0 / 56 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort B: Period 3 Placebo From High Dose	Cohort B: Period 3 OM Low Dose Continued	Cohort B: Period 3 OM High Dose Continued
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	4 / 26 (15.38%)
Investigations			
Blood urea increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Diarrhea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Rhinorrhea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Proteinurea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tonsilitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort C: Period 3 Placebo From OM in Period 2	Cohort B: Period 3 Placebo From Low Dose	Cohort B: Period 4 Open-label OM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 29 (27.59%)	1 / 26 (3.85%)	56 / 104 (53.85%)
Investigations			
Blood urea increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	1	0	4
Headache			
subjects affected / exposed	0 / 29 (0.00%)	1 / 26 (3.85%)	18 / 104 (17.31%)
occurrences (all)	0	1	38
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	9 / 104 (8.65%)
occurrences (all)	0	0	15
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	7 / 104 (6.73%)
occurrences (all)	0	0	7
Diarrhea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	3 / 104 (2.88%)
occurrences (all)	1	0	3
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	3 / 104 (2.88%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	7 / 104 (6.73%)
occurrences (all)	1	0	8
Rhinorrhea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	0	0	2
Epistaxis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	5 / 104 (4.81%)
occurrences (all)	0	0	5
Nasal congestion			

subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	0	0	2
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	2 / 104 (1.92%)
occurrences (all)	0	0	0
Proteinurea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 26 (0.00%)	4 / 104 (3.85%)
occurrences (all)	2	0	6
Upper respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	3 / 104 (2.88%)
occurrences (all)	0	0	6
Influenza			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	4 / 104 (3.85%)
occurrences (all)	1	0	4
Pharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Tonsilitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			

subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 26 (0.00%)	0 / 104 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Cohort C: Period 2 Open-label OM	Cohort C: Period 3 OM Dose Continued	Cohort C: Period 4 Open-label OM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 59 (20.34%)	4 / 29 (13.79%)	46 / 57 (80.70%)
Investigations			
Blood urea increased			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 59 (1.69%)	0 / 29 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 59 (5.08%)	0 / 29 (0.00%)	7 / 57 (12.28%)
occurrences (all)	3	0	8
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Diarrhea			

subjects affected / exposed	1 / 59 (1.69%)	0 / 29 (0.00%)	4 / 57 (7.02%)
occurrences (all)	1	0	5
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	3 / 59 (5.08%)	1 / 29 (3.45%)	5 / 57 (8.77%)
occurrences (all)	3	1	6
Rhinorrhea			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	3
Nasal congestion			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	8
Rhinitis			
subjects affected / exposed	0 / 59 (0.00%)	2 / 29 (6.90%)	4 / 57 (7.02%)
occurrences (all)	0	2	4
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	7
Proteinurea			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 29 (0.00%)	2 / 57 (3.51%)
occurrences (all)	1	0	2
Upper respiratory tract infection			

subjects affected / exposed	1 / 59 (1.69%)	1 / 29 (3.45%)	11 / 57 (19.30%)
occurrences (all)	1	1	15
Influenza			
subjects affected / exposed	1 / 59 (1.69%)	1 / 29 (3.45%)	3 / 57 (5.26%)
occurrences (all)	1	1	3
Pharyngitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Otitis media acute			
subjects affected / exposed	1 / 59 (1.69%)	0 / 29 (0.00%)	3 / 57 (5.26%)
occurrences (all)	1	0	4
Tonsilitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	8
Urinary tract infection			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	4
Viral infection			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Metabolism and nutrition disorders			
Pseudohyperkalemia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 29 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2005	The amendment was included to increase the number of subjects in Cohort C from 50 to 60, added glomerular kidney disease to the definition of subjects with hypertension as greater than or equal to (>=)90th percentile in the inclusion criteria, added greater than (>) 2 standard deviation (SD) to the exclusion criteria for seated systolic blood pressure (SeSBP) / seated diastolic blood pressure (SeDBP) in subjects with malignant hypertension, changed the primary efficacy analysis to include the change from baseline in SeDBP, and amended statistical analyses to include examination of Cohorts A, B, and A + B combined.
06 March 2006	The amendment was included to clarified conditions for interpretation of screening potassium levels, added angiotensin converting enzyme (ACE) inhibitors as an excluded antihypertensive medication during Period IV, added SeDBP to the definition of malignant hypertension, and identified the central clinical laboratory.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported