Clinical trial results:
An Open-label Study of the Single-dose Pharmacokinetics of Olmesartan Medoxomil in Pediatric Patients With Hypertension

Summary

EudraCT number	2015-003328-30
Trial protocol	Outside EU/EEA
Global end of trial date	06 February 2008

Results information

Result version number	v1 (current)
This version publication date	20 November 2018
First version publication date	02 September 2016

Trial information

Trial identification

Sponsor protocol code	CS0866-A-U102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00151814
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo Pharma Development
Sponsor organisation address	399 Thornall Street, Edison, United States, 08837
Public contact	Daiichi Sankyo Pharma Development, 399 Thornall Street, Edison, NJ 08837, United States, Jason Mann, +001 732 5905011, jamann@dsi.com
Scientific contact	Daiichi Sankyo Pharma Development, 399 Thornall Street, Edison, NJ 08837, United States, Jason Mann, +001 732 5905011, jamann@dsi.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	06 February 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 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 determine the single-dose Pharmacokinetics of olmesartan following oral administration of a pro-drug, Olmesartan medoxomil (OM), in pediatric subjects with hypertension ages 12 months to 16 years.

Protection of trial subjects:

The safety assessments included clinical laboratory tests (hematology, serum chemistry and urinalysis), Electrocardiogram, Physical examination findings and Vital signs. Adverse events were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 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: 24
Worldwide total number of subjects	24
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	14
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment period was from September 2005 to February 2008. This period lasted for this length of time because of difficulties in recruiting subjects. Children from 12 months old to 16 years old were to be enrolled.

Pre-assignment

Screening details:

A total of 33 subjects were screened, of these 24 subjects were enrolled and completed the study. No subjects in the 12-23 month old category were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olmesartan Group - 2 to 5 years old

Arm description:

Subjects who were less than (<) 6 years old received single dose of Olmesartan medoxomil oral suspension, 0.3 milligram per kilogram body weight (mg/kg).

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

Dosage and administration details:

Subjects received single dose of Olmesartan Medoxomil oral suspension at a dose of 0.3 mg/kg.

Arm title	Olmesartan Group - 6 to 12 Years Old

Arm description:

Subjects who were greater than or equal to (> =) 6 to 12 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight less than (<) 35 kg the dose was 20 mg tablet.

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	Benicar
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were greater than or equal to (> =) 6 to 12 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight less than (<) 35 kg the dose was 20 mg tablet.

Arm title	Olmesartan Group - 13 to 16 Years Old

Arm description:

Subjects who were > = 13 to 16 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight < 35 kg the dose was 20 mg tablet.

Arm type	Experimental

Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	Benicar
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were > = 13 to 16 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight < 35 kg the dose was 20 mg tablet.

Number of subjects in period 1	Olmesartan Group - 2 to 5 years old	Olmesartan Group - 6 to 12 Years Old	Olmesartan Group - 13 to 16 Years Old
Started	4	10	10
Completed	4	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Olmesartan Group - 2 to 5 years old
Reporting group description:	
Subjects who were less than (<) 6 years old received single dose of Olmesartan medoxomil oral suspension, 0.3 milligram per kilogram body weight (mg/kg).	
Reporting group title	Olmesartan Group - 6 to 12 Years Old
Reporting group description:	
Subjects who were greater than or equal to (> =) 6 to 12 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight less than (<) 35 kg the dose was 20 mg tablet.	
Reporting group title	Olmesartan Group - 13 to 16 Years Old
Reporting group description:	
Subjects who were > = 13 to 16 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight < 35 kg the dose was 20 mg tablet.	

Reporting group values	Olmesartan Group - 2 to 5 years old	Olmesartan Group - 6 to 12 Years Old	Olmesartan Group - 13 to 16 Years Old
Number of subjects	4	10	10
Age categorical Units: Subjects			
Children (2-11 years)	4	10	0
Adolescents (12-17 years)	0	0	10
Age continuous Units: years			
arithmetic mean	4.8	10.2	14.8
standard deviation	± 0.5	± 1.03	± 1.03
Gender categorical Units: Subjects			
Female	3	5	5
Male	1	5	5
Height Units: centimeter (cm)			
arithmetic mean	116.7	151.8	165.5
standard deviation	± 9.01	± 9.44	± 9.74
Weight Units: kilogram (kg)			
arithmetic mean	32	70.3	86.3
standard deviation	± 16.31	± 20.53	± 29.5

Reporting group values	Total		
Number of subjects	24		
Age categorical Units: Subjects			
Children (2-11 years)	14		
Adolescents (12-17 years)	10		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	13		
Male	11		
Height Units: centimeter (cm) arithmetic mean standard deviation	- -		
Weight Units: kilogram (kg) arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Olmesartan Group - 2 to 5 years old
Reporting group description:	
Subjects who were less than (<) 6 years old received single dose of Olmesartan medoxomil oral suspension, 0.3 milligram per kilogram body weight (mg/kg).	
Reporting group title	Olmesartan Group - 6 to 12 Years Old
Reporting group description:	
Subjects who were greater than or equal to (> =) 6 to 12 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight less than (<) 35 kg the dose was 20 mg tablet.	
Reporting group title	Olmesartan Group - 13 to 16 Years Old
Reporting group description:	
Subjects who were > = 13 to 16 years old, with weight > or = 35 kg received single oral dose of Olmesartan medoxomil, 40 mg tablet; for subjects with weight < 35 kg the dose was 20 mg tablet.	

Primary: Area Under the Concentration-time Curve From Time 0 to Time of last Quantifiable Concentration (AUC 0-t) of Olmesartan

End point title	Area Under the Concentration-time Curve From Time 0 to Time of last Quantifiable Concentration (AUC 0-t) of Olmesartan[1][2]
End point description:	
The AUC(0-last) is the area under the plasma concentration-time curve from time zero to last quantifiable concentration. Pharmacokinetic population included all randomized subjects who received study drug. The data for 2-5 years old subjects were not analyzed.	
End point type	Primary
End point timeframe:	
Pre-dose and 1,2,4,8,12,24,48 hours post-dose	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Olmesartan Group - 2-5 years old subjects were not analyzed due to insufficient number of subjects.

End point values	Olmesartan Group - 6 to 12 Years Old	Olmesartan Group - 13 to 16 Years Old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram per millilitre *hour (ng/mL*hr)				
arithmetic mean (standard deviation)	7874 (± 2913)	5851 (± 2083)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Olmesartan

End point title	Area Under the Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Olmesartan[3][4]

End point description:

The AUC (0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. Pharmacokinetic population included all randomized subjects who received study drug. The data for 2-5 years old subjects were not analyzed.

End point type	Primary

End point timeframe:

Pre-dose and 1,2,4,8,12,24,48 hours post-dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Olmesartan Group - 2-5 years old subjects were not analyzed due to insufficient number of subjects.

End point values	Olmesartan Group - 6 to 12 Years Old	Olmesartan Group - 13 to 16 Years Old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: ng/mL*hr				
arithmetic mean (standard deviation)	7988 (± 2913)	5982 (± 2130)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Olmesartan

End point title	Maximum Plasma Concentration (Cmax) of Olmesartan[5][6]

End point description:

The Cmax is the maximum observed plasma concentration of Olmesartan. Pharmacokinetic population included all randomized subjects who received study drug. The data for 2-5 years old subjects were not analyzed.

End point type	Primary

End point timeframe:

Pre-dose and 1,2,4,8,12,24,48 hours post-dose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The data for Olmesartan Group - 2-5 years old subjects were not analyzed due to insufficient number of subjects.

End point values	Olmesartan Group - 6 to 12 Years Old	Olmesartan Group - 13 to 16 Years Old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanogram(s)/milliliter (ng/mL)				
arithmetic mean (standard deviation)	1227 (± 451)	895 (± 262)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From First administration of study drug up to 48 hours Post-dose

Adverse event reporting additional description:

Adverse events observed by the Investigator, or reported by the subject, and any remedial action taken, were recorded in case report form by 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	Olmesartan Group - 2 to 5 years old

Reporting group description:

Subjects who were less than (<) 6 years old received single dose of Olmesartan medoxomil oral suspension, 0.3 milligram per kilogram body weight (mg/kg).

Reporting group title	Olmesartan Group - 13 to 16 Years Old

Reporting group description:

Subjects who were greater than or equal to (> =) 13 to 16 years old; > or = 35 kg weight was received single oral dose of Olmesartan medoxomil, 40 mg tablet; for < 35 kg the dose was 20 mg tablet.

Reporting group title	Olmesartan Group - 6 to 12 Years Old

Reporting group description:

Subjects who were greater than or equal to (> =) 6 to 12 years old; > or = 35 kg weight was received single oral dose of Olmesartan medoxomil, 40 mg tablet; for < 35 kg the dose was 20 mg tablet.

Serious adverse events	Olmesartan Group - 2 to 5 years old	Olmesartan Group - 13 to 16 Years Old	Olmesartan Group - 6 to 12 Years Old
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Olmesartan Group - 2 to 5 years old	Olmesartan Group - 13 to 16 Years Old	Olmesartan Group - 6 to 12 Years Old
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	2 / 10 (20.00%)
Investigations			
Abnormal urine analysis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Diarrhea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported