Clinical trial results:
An Open-label Extension Study of Candesartan Cilexetil in Hypertensive Pediatric Subjects Ages 1 to <11 Years: A Long-term Study

Summary

EudraCT number	2007-001545-17
Trial protocol	DE BE FR PL IT
Global end of trial date	09 September 2009

Results information

Result version number	v1 (current)
This version publication date	16 April 2016
First version publication date	16 April 2016

Trial information

Trial identification

Sponsor protocol code	D2451C00006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00690612
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Pepparedsleden 1, Molndal, Sweden, 431 83
Public contact	Robin Mukherjee, R&D/GMD/Biometrics & Information Sciences, robin.mukherjee@astrazeneca.com
Scientific contact	Robin Mukherjee, R&D/GMD/Biometrics & Information Sciences, robin.mukherjee@astrazeneca.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	09 September 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2009
Global end of trial reached?	Yes
Global end of trial date	09 September 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to describe the long-term clinical experience of candesartan cilexetil in hypertensive children ages 1 to <11 years who had participated in Protocol 328 (D2451C00002) without discontinuation due to a study drug-related AE, and who had an ongoing clinical indication for treatment with candesartan cilexetil.

Protection of trial subjects:

The study ICI and the AstraZeneca Study Physician reviewed and discussed each SAE. In addition, an independent pediatric hypertension expert not otherwise participating in the study reviewed all SAEs, AEs, and AEs leading to discontinuation (DAEs) of the study drug. The safety committee consisting of the ICI and the independent expert met 3 times; minutes from the meetings are archived with the sponsor.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Ukraine: 5
Worldwide total number of subjects	35
EEA total number of subjects	30

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	0

months)	
Children (2-11 years)	35
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Hypertensive children aged 1 to <11 years who had participated in the 1-year study (Protocol 328, D2451C00002-NCT00244621). First patient enrolled 17 Sep 2007 and last patient completed 9 Sep 2009 at Pediatric clinics in Europe.

Pre-assignment

Screening details:

Patients who had participated in the 1-year study (Protocol 328, D2451C00002-NCT00244621) and did not discontinue study due to a study drug-related adverse event (AE) and had an ongoing clinical indication for treatment with candesartan.

Period 1

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

Arms

Arm title	Overall

Arm description:

Overall

Arm type	Follow-up
Investigational medicinal product name	Candesartan Cilexetil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

0.05, 0.20 and 0.40 mg

Number of subjects in period 1	Overall
Started	35
Completed	32
Not completed	3
Consent withdrawn by subject	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	35	35	
Age categorical Units: Subjects			
2-5	24	24	
6-11	11	11	
Age Continuous | Units: Years			
arithmetic mean	4.4		
standard deviation	± 1.6	-	
Gender, Male/Female Units: participants			
Female	10	10	
Male	25	25	

End points

End points reporting groups

Reporting group title	Overall
Reporting group description:	
Overall	

Primary: Mean change from baseline to final visit in systolic blood pressure (SBP).

End point title	Mean change from baseline to final visit in systolic blood pressure (SBP).[1]
End point description:	
Blood pressure response was defined as Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) less than the 95th percentile based on population height-adjusted charts for age and gender. Response rates were based on the proportion of patients meeting the criteria at each evaluation time point or the last available measure.	
End point type	Primary
End point timeframe:	
Every 3 months- baseline to final visit	

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: No statistical analyses in the sense of hypothesis testing were carried out for the primary endpoints.

End point values	Overall			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Millimeters of Mercury (mm Hg)				
arithmetic mean (standard deviation)	-2.86 (± 11.97)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean change from baseline to final visit in diastolic blood pressure (DBP).

End point title	Mean change from baseline to final visit in diastolic blood pressure (DBP).[2]
End point description:	
Blood pressure response was defined as Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) less than the 95th percentile based on population height-adjusted charts for age and gender. Response rates were based on the proportion of patients meeting the criteria at each evaluation time point or the last available measure.	
End point type	Primary
End point timeframe:	
every 3 months - baseline to final visit	

Notes:

[2] - 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: No statistical analyses in the sense of hypothesis testing were carried out for the primary endpoint.

End point values	Overall			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mm Hg				
arithmetic mean (standard deviation)	-0.43 (± 12.26)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the entire study period; from 14 days before patient received study medication to end of study (month 27).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	NA

Reporting groups

Reporting group title	Atacand candesartan cilexetil

Reporting group description:

candesartan cilexetil (Atacand) approximately 0.05 mg/kg, 0.2 mg/kg, and 0.4 mg/kg doses administered in oral suspension form.

Serious adverse events	Atacand candesartan cilexetil		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 35 (8.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Lymphoedema			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
alternative dictionary used: MedDRA 10.0			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Atacand candesartan cilexetil		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 35 (80.00%)		
General disorders and administration site conditions			
PYREXIA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	9 / 35 (25.71%)		
occurrences (all)	9		
FATIGUE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	6		
Nausea			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
VOMITING			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
COUGH			
alternative dictionary used: MedDRA 10.0			

subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	5		
UPPER RESPIRATORY TRACT INFLAMMATION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Renal and urinary disorders			
ENURESIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Infections and infestations			
PHARYNGITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	6		
RHINITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	6		
NASOPHARYNGITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
BRONCHITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
UPPER RESPIRATORY TRACT INFECTION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
VARICELLA			
alternative dictionary used: MedDRA 10.0			

subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
ACUTE TONSILLITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
GASTROENTERITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
INFLUENZA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
OTITIS MEDIA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
OTITIS MEDIA ACUTE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
TONSILLITIS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
URINARY TRACT INFECTION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2007	Echocardiography (ECHO) is added following recommendation from the Paedeatric Committee (PDCO) at the European Medicines Agency's (EMEA).
11 February 2008	The investigator or designated cardiologist will perform an echocardiogram (ECHO) at study entry and then annually during the course of this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported