



Clinical trial results:

Dose Titration of Lisinopril in Children Aged 1 to 18 Years With Primary or Secondary Hypertension

Summary

EudraCT number	2012-002927-14
Trial protocol	BE
Global end of trial date	14 June 2018

Results information

Result version number	v1 (current)
This version publication date	07 June 2024
First version publication date	07 June 2024
Summary attachment (see zip file)	Final Study Report (2012-498_Final Study Report_20181218.pdf) Protocol (2012-002927-14_Protocol version 3.0_20130214.pdf)

Trial information

Trial identification

Sponsor protocol code	AGO/2012/004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02184858
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UZ Ghent
Sponsor organisation address	Corneel Heymanslaan 10, 9000, Belgium, Ghent
Public contact	Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be
Scientific contact	Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 May 2017
Global end of trial reached?	Yes
Global end of trial date	14 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy and safety of lisinopril in children aged 1 to 18 years with both primary and secondary hypertension.

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 August 2012
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	Belgium: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	6
Adolescents (12-17 years)	7
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

13 patients were recruited between 25-JUN-2014 and 08-May-2017. End of trial notification was dated 14-Jun-2018 (last patient last visit) and submitted to EC and CA on 17-Sep-2018. There were no dropouts.

Pre-assignment

Screening details:

Patients between 1 and 18 years with a systolic and/or diastolic blood pressure above the 95th percentile for their age without reversible cause were included. Patients were screened as per inclusion and exclusion criteria in the protocol.

Period 1

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

Blinding implementation details:

Open label trial

Arms

Are arms mutually exclusive?	No
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Arm title	Baseline data
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Arm description:

Baseline data of patients enrolled in the trial

Arm type	Baseline arm
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No investigational medicinal product assigned in this arm

Arm title	Active arm
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Arm description:

Active arm with lisinopril administration

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

Dosage and administration details:

Start dose of 0.1mg/kg/day with monthly uptitration with 0.1mg/kg/day until a maximal dose of 0.4mg/kg/day.

In case of GFR >30-60ml/min: Start dose of 0.05mg/kg/day with monthly uptitration with 0.05mg/kg/day until a maximal dose of 0.2mg/kg/day.

In case of GFR >30-60ml/min: Start dose of 0.025mg/kg/day with monthly uptitration with 0.025mg/kg/day until a maximal dose of 0.1mg/kg/day.

In case of GFR >30-60ml/min: Start dose of 0.0125mg/kg/day with monthly uptitration with 0.0125mg/kg/day until a maximal dose of 0.05mg/kg/day.

Patients already on lisinopril treated with a study dose closest to their current dose and will start at visit 2, 4 or 6 depending on the start dose.

Number of subjects in period 1	Baseline data	Active arm
Started	13	13
Completed	13	13

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	13	13	
Age categorical			
Subject age at start of trial			
Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	6	6	
Adolescents (12-17 years)	7	7	
Gender categorical			
Gender			
Units: Subjects			
Female	4	4	
Male	9	9	
Race			
Race			
Units: Subjects			
Caucasian	12	12	
African	1	1	
Lisinopril at baseline			
To define if patients were already using lisinopril at baseline or not			
Units: Subjects			
Lisinopril at baseline	2	2	
No lisinopril at baseline	11	11	
Kidney disease			
Kidney disease and need for dose reduction defined by the protocol			
Units: Subjects			
No kidney disease	10	10	
Kidney disease, no dose reduction	1	1	
Kidney disease, dose reduction	2	2	

End points

End points reporting groups

Reporting group title	Baseline data
Reporting group description: Baseline data of patients inrolled in the trial	
Reporting group title	Active arm
Reporting group description: Active arm with lisinopril administration	

Primary: Reaching target blood pressure by personalized lisinopril dosing

End point title	Reaching target blood pressure by personalized lisinopril
End point description:	
End point type	Primary
End point timeframe:	
Dose is increased to a maximum over the period of 4 weeks or untill hypotension would occur	
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: See attachments	

End point values	Baseline data	Active arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: dose				
number (not applicable)	13	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose-response correlation

End point title	Dose-response correlation
End point description:	
End point type	Secondary
End point timeframe:	
continuous monitoring during the course of the study	

End point values	Baseline data	Active arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: nap				
number (not applicable)	13	13		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From start until end of study.

Only SAEs were reported

Adverse event reporting additional description:

Only SAEs were reported

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Overall trial
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Reporting group description:

All subjects in the trial

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were recorded for the participating patients

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Colitis	Additional description: Hospitalisation due to colitis		
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pelvi-ureteric obstruction	Additional description: Hospitalisation with correction		
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the strict GMP legislation, the magistral preparation of lisinoprii became too labor intensive

Notes: