# 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)<br>Protocol (2012-002927-14_Protocol version 3.0_20130214.pdf) |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | AGO/2012/004 |

### 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 abd 08-May-2017. End of trial notification was dated 14-Jun-2018(last patient last visit) and submitted to EC and CA on17-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 rversible 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 |
| **Arm title** | Baseline data |

Arm description:

Baseline data of patients inrolled in the trial

| | |
|---|---|
| Arm type | Baseline arm |

No investigational medicinal product assigned in this arm

| | |
|---|---|
| **Arm title** | Active arm |

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.<br>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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Overall trial |

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: