# Clinical trial results:
# Pharmacokinetics of ciprofloxacine in pediatric patients, a pilot study – SAFE PEDRUG

## Summary

| | |
|---|---|
| EudraCT number | 2014-004638-24 |
| Trial protocol | BE |
| Global end of trial date | 17 March 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 April 2022 |
| First version publication date | 03 April 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SafePed01 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02598362 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Ghent University Hospital |
| Sponsor organisation address | C. 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 | 06 September 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 March 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 March 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Investigating the feasibility of a study method for pharmacokinetics (with emphasis on renal clearance) of ciprofloxacin in children.

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 | 28 May 2015 |
| 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: 23 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 23 |

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) | 3 |
| Children (2-11 years) | 10 |
| 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:

23 patients were included starting from 28-May-2015. End of trial notification was dated 17-Mar-2018 (last patient last visit) and submitted to EC and CA on 28/08/2018.

### Pre-assignment

Screening details:

fUTI group (UZ Brussels): patients aged 3 months-17years with rectal temperature of 38.5°C and significant leucocyturia or a positive urine nitrite test in a sterile urine sample and confirmed by culture. Profylaxis group (UZ Ghent): patients until age of 17years who use cipro for preventing urinary tract infectons.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (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** | fUTI arm (IV arm) |

Arm description:

UZ Brussels patients aged 3 months-17years with rectal temperature of 38.5°C and significant leucocyturia or a positive urine nitrite test in a sterile urine sample and confirmed by culture.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ciprofloxacin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

15mg/kg twice daily

| | |
|---|---|
| **Arm title** | Profylaxis arm (oral arm) |

Arm description:

UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infectons.
Oral administration

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Ciprofloxacin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Normal dose (usual 10mg/kg daily)

| **Number of subjects in period 1** | fUTI arm (IV arm) | Profylaxis arm (oral arm) |
|---|---|---|
| Started | 10 | 13 |
| Completed | 10 | 13 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | fUTI arm (IV arm) |
| Reporting group description: | |
| UZ Brussels patients aged 3 months-17years with rectal temperature of 38.5°C and significant leucocyturia or a positive urine nitrite test in a sterile urine sample and confirmed by culture. | |
| Reporting group title | Profylaxis arm (oral arm) |
| Reporting group description: | |
| UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infectons. Oral administration | |

| Reporting group values | fUTI arm (IV arm) | Profylaxis arm (oral arm) | Total |
|---|---|---|---|
| Number of subjects | 10 | 13 | 23 |
| Age categorical<br>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<br>Units: years | | | |
| median | 9.86 | 6.43 | |
| full range (min-max) | 0.51 to 15.5 | 0.31 to 15.4 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 8 | 6 | 14 |
| Male | 2 | 7 | 9 |
| Diagnose<br>Units: Subjects | | | |
| Acute pyelonephritis | 9 | 9 | 18 |
| Cystitis | 1 | 2 | 3 |
| recurrent lower UTI | 0 | 2 | 2 |
| Comorbidities<br>Units: Subjects | | | |
| CAKUT | 3 | 7 | 10 |
| Neurogenic bladder | 1 | 0 | 1 |
| BBD | 2 | 1 | 3 |
| CAKUT and stone disease | 1 | 1 | 2 |
| CAKUT and renal insufficiency | 0 | 1 | 1 |
| CAKUT and BBD | 0 | 1 | 1 |
| stone disease | 0 | 1 | 1 |
| None | 3 | 1 | 4 |

| | | | |
|---|---|---|---|
| Urine culture<br>Units: Subjects | | | |
| Escherichia coli | 4 | 5 | 9 |
| Pseudomonas aeruginosa | 3 | 4 | 7 |
| Klebsiella pneumoniae | 1 | 1 | 2 |
| Proteus strains | 0 | 1 | 1 |
| No growth | 2 | 2 | 4 |
| Weight<br>Units: kg | | | |
| median | 26.7 | 18.3 | |
| full range (min-max) | 8.21 to 75.30 | 6.47 to 106 | - |
| Serum cystatin C<br>Units: mg/l | | | |
| median | 0.71 | 0.86 | |
| full range (min-max) | 0.63 to 0.84 | 0.61 to 2.88 | - |
| Serum creatinine<br>Units: mg/dl | | | |
| median | 0.49 | 0.64 | |
| full range (min-max) | 0.28 to 0.81 | 0.38 to 1.54 | - |
| Kidney function<br>Units: ml/min/1.73m² | | | |
| median | 98.4 | 65.5 | |
| full range (min-max) | 73.7 to 116 | 6.75 to 84.6 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | fUTI arm (IV arm) |
| Reporting group description: | |
| UZ Brussels patients aged 3 months-17years with rectal temperature of 38.5°C and significant leucocyturia or a positive urine nitrite test in a sterile urine sample and confirmed by culture. | |
| Reporting group title | Profylaxis arm (oral arm) |
| Reporting group description: | |
| UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infectons.<br>Oral administration | |
| Subject analysis set title | End group |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Group created as data are analysed as a one armed trial. | |

### Primary: ciprofloxacin clearance

| | |
|---|---|
| End point title | ciprofloxacin clearance[1] |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| From start until end of study | |
| 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 article | |

| End point values | End group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: l/h/kg | | | | |
| median (full range (min-max)) | 0.22 (0.16 to 0.43) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Volume of distribution

| | |
|---|---|
| End point title | Volume of distribution |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| From start until end of study | |

| End point values | End group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: l/kg | | | | |
| median (full range (min-max)) | 0.55 (0.06 to 2.88) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Bioavailibility

| End point title | Bioavailibility |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From start until end study

| End point values | End group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: percentage | | | | |
| number (not applicable) | 59.6 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: absorption

| End point title | absorption |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From start until end study

| End point values | End group | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: per hour | | | | |
| number (not applicable) | 0.596 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events will be reported between the first dose administration of trial medication and the last trial related activity

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

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

### Reporting groups

| | |
|---|---|
| Reporting group title | fUTI arm (IV arm) |

Reporting group description:

UZ Brussels patients aged 3 months-17years with rectal temperature of 38.5°C and significant leucocyturia or a positive urine nitrite test in a sterile urine sample and confirmed by culture.

| | |
|---|---|
| Reporting group title | Profylaxis arm (oral arm) |

Reporting group description:

UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infectons.
Oral administration

| Serious adverse events | fUTI arm (IV arm) | Profylaxis arm (oral arm) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 13 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | fUTI arm (IV arm) | Profylaxis arm (oral arm) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 13 (0.00%) | |

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 adverse events have been collected

## 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

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/29987142