



## Clinical trial results:

### Pharmacokinetics of ciprofloxacin 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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| 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:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 23 |
| Worldwide total number of subjects   | 23          |
| EEA total number of subjects         | 23          |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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. Prophylaxis group (UZ Ghent): patients until age of 17years who use cipro for preventing urinary tract infections.

### 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               |
| <b>Arm title</b>             | 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

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Prophylaxis arm (oral arm) |
|------------------|----------------------------|

Arm description:

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

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)

| <b>Number of subjects in period 1</b> | 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:<br>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:<br>UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infectons.<br>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                    |               |              |   |
| 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                           |               |              |   |
| Units: kg                        |               |              |   |
| median                           | 26.7          | 18.3         |   |
| full range (min-max)             | 8.21 to 75.30 | 6.47 to 106  | - |
| Serum cystatin C                 |               |              |   |
| Units: mg/l                      |               |              |   |
| median                           | 0.71          | 0.86         |   |
| full range (min-max)             | 0.63 to 0.84  | 0.61 to 2.88 | - |
| Serum creatinine                 |               |              |   |
| Units: mg/dl                     |               |              |   |
| median                           | 0.49          | 0.64         |   |
| full range (min-max)             | 0.28 to 0.81  | 0.38 to 1.54 | - |
| Kidney function                  |               |              |   |
| Units: ml/min/1.73m <sup>2</sup> |               |              |   |
| 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:<br>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:<br>UZ Ghent patients until age of 17years who use cipro for preventing urinary tract infections.<br>Oral administration   |                           |
| Subject analysis set title   | End group                 |
| Subject analysis set type  | Per protocol              |
| Subject analysis set description:<br>Group created as data are analysed as a one armed trial.  |                           |

### Primary: ciprofloxacin clearance

|   |  |
|---|--|
| End point title   | ciprofloxacin clearance <sup>[1]</sup> |
| End point description:  |  |
| End point type  | Primary                                |
| End point timeframe:<br>From start until end of study   |  |
| Notes:<br>[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:<br>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: Bioavailability

|                            |                 |
|----------------------------|-----------------|
| End point title            | Bioavailability |
| 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 |            |



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

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

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 infections.  
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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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