



Clinical trial results:

Study of the pharmacokinetics and pharmacodynamics of desmopressin oral lyophilisate - route of administration in the pediatric patient population - SAFEPEDRUG

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-005200-13 |
| Trial protocol | BE |
| Global end of trial date | 31 December 2018 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 19 August 2021 |
| First version publication date | 19 August 2021 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | SafePed002 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02584231 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Ghent University Hospital |
| Sponsor organisation address | C. Heymanslaan 10, Ghent, Belgium, 9000 |
| 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 | 01 February 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 March 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the influence of the weight, length and gender on the pharmacokinetics of desmopressin

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 | 01 July 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: 25 |
| Worldwide total number of subjects | 25 |
| EEA total number of subjects | 25 |

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) | 22 |
| 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:

25 patients were recruited between 09-09-2015 and 19-03-2018. End of trial notification was dated 31-12-2018 (last patient last visit) and submitted to EC and CA on 09-01-2019. There were 2 dropouts due to technical problems with blood sampling.

Pre-assignment

Screening details:

The following groups were included in the study: between 6 months and 2 years (n=3): dosing with 60µg of PO; between 2 and 4 years (n=5): dosing with 120µg PO and between 4 and 8 years (n=17): dosage with 240 µg PO.

Period 1

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

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | No |
| Arm title | Desmopressine arm |

Arm description:

Treatment of enuresis nocturna in paediatric patients, with desmopressine lyophilisaat (MELT) 60 or 120µg for oral use.

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Desmopressine |
| Investigational medicinal product code | CAS 16679-58-6 |
| Other name | Minirin Melt |
| Pharmaceutical forms | Oral lyophilisate, Tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

Doses are administered according to the patient's age: between 6 months and 2 years: dosing with 60µg of PO; between 2 and 4 years: dosing with 120µg PO and between 4 and 8 years: dosage with 240 µg PO.

| | |
|------------------|--------------|
| Arm title | Baseline arm |
|------------------|--------------|

Arm description:

Baseline data for the study, as the study only has 1 arm

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

| Number of subjects in period 1 | Desmopressine arm | Baseline arm |
|---|-------------------|--------------|
| Started | 25 | 25 |
| Completed | 23 | 25 |
| Not completed | 2 | 0 |
| technical problems with blood sampling. | 2 | - |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 25 | 25 | |
| Age categorical | | | |
| Treatment of enuresis nocturna in paediatric patients (age 0,9 - 7,3 years). | | | |
| Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 3 | 3 | |
| Children (2-11 years) | 22 | 22 | |
| Gender categorical | | | |
| All 25 patients, 9 girls and 16 boys, completed the renal concentrating test. | | | |
| Units: Subjects | | | |
| Female | 9 | 9 | |
| Male | 16 | 16 | |
| Weight | | | |
| Units: kg | | | |
| median | 17.8 | | |
| inter-quartile range (Q1-Q3) | 13.0 to 25.5 | - | |
| Length | | | |
| Units: cm | | | |
| median | 112 | | |
| inter-quartile range (Q1-Q3) | 95.6 to 123 | - | |
| BMI | | | |
| Units: kg/m ² | | | |
| median | 1.56 | | |
| inter-quartile range (Q1-Q3) | 1.51 to 1.66 | - | |
| Dose/weight | | | |
| Units: µg/kg | | | |
| median | 9.41 | | |
| inter-quartile range (Q1-Q3) | 8.57 to 11.8 | - | |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | Desmopressine arm |
| Reporting group description: Treatment of enuresis nocturna in paediatric patients, with desmopressine lyophilisaat (MELT) 60 or 120µg for oral use. | |
| Reporting group title | Baseline arm |
| Reporting group description: Baseline data for the study, as the study only has 1 arm | |

Primary: Desmopressine concentrations

| | |
|------------------------|--|
| End point title | Desmopressine concentrations ^{[1][2]} |
| End point description: | |

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

0, 1/4, 1/2, 1, 2, 3, 5, 6 and 7h

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 analysis available.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm).

| | | | | |
|-------------------------------|-------------------|--|--|--|
| End point values | Desmopressine arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 ^[3] | | | |
| Units: pg*h/mL | | | | |
| median (full range (min-max)) | | | | |
| AUC (0 - infinity) | 105 (66 to 146) | | | |

Notes:

[3] - No PK data available for the first 5 of the 25 patients (technical problem storage conditions)

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - osmolality in urine

| | |
|-----------------|---|
| End point title | Efficacy - osmolality in urine ^[4] |
|-----------------|---|

End point description:

PD of desmopressin in children with nocturnal enuresis that is resistant to treatment with desmopressin tablet. Second PD parameter is urinary concentration capacity. This is osmolality in urine.

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

End point timeframe:

24 hours

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm).

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Desmopressine arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: mOsm/kg | | | | |
| arithmetic mean (standard deviation) | 859 (± 67) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Safety of desmopressin in children as assessed by registration of adverse events.

| | |
|-----------------|--|
| End point title | Safety of desmopressin in children as assessed by registration of adverse events. ^[5] |
|-----------------|--|

End point description:

Registration of adverse events

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

End point timeframe:

24 hours

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm).

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Desmopressine arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: adverse events | | | | |
| occurrence of adverse events | 4 | | | |
| occurrence of serious adverse events | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Safety of desmopressin in children as assessed by the measurement of natremia

| | |
|-----------------|--|
| End point title | Safety of desmopressin in children as assessed by the measurement of natremia ^[6] |
|-----------------|--|

End point description:

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 24 hours | |
| Notes: | |
| [6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm). | |

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Desmopressine arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: sodium (plasma, mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| difference in sodium (plasma) | 0.5 (± 2.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - urinary volume.

| | |
|--|---|
| End point title | Efficacy - urinary volume. ^[7] |
| End point description: | |
| Antidiuretic effect was defined in this study if the diuresis rate dropped below 2mL/kg/h (age c 2 y) or 1 mL/kg/h (age > 2y) | |
| End point type | Secondary |
| End point timeframe: | |
| 24 hours | |
| Notes: | |
| [7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm). | |

| | | | | |
|--|-------------------|--|--|--|
| End point values | Desmopressine arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 | | | |
| Units: patients with antidiuretic effect (n) | | | | |
| drop below 2mL/kg/h (<2y) or 1 mL/kg/h (>2y) | 10 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary concentration test

| | |
|-----------------|---|
| End point title | Urinary concentration test ^[8] |
|-----------------|---|

End point description:

Evaluation of the oral lyophilisate formulation of desmopressin for the urinary concentration test

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

End point timeframe:

24 hours

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistics are not reported for the baseline arm (baseline arm for the study, as the study only has 1 arm).

| End point values | Desmopressine arm | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 ^[9] | | | |
| Units: mL/min/kg | | | | |
| arithmetic mean (standard deviation) | 0.76 (± 0.46) | | | |

Notes:

[9] - No PK data available for the first 5 of the 25 patients (technical problem storage conditions)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

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 | 24 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Trial |
|-----------------------|---------------|

Reporting group description:

Treatment of enuresis nocturna in paediatric patients, with desmopressine lyophilisaat (MELT) 60 or 120µg for oral use.

| Serious adverse events | Overall Trial | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Overall Trial | | |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| General disorders and administration site conditions | | | |
| sore throat | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |
| abdominal pain/stomach pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|---------------------|--|--|
| Renal and urinary disorders pain during voiding subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | | |
|--|---------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 21 January 2016 | Reason for substantial amendment: <ul style="list-style-type: none">• Removal of Tanner stage determination from protocol.• Correction of typing error• Extra measurement of Desmopressin concentration in urine |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported