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 pharmacokinetcs 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/m²			
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				
occurence of adverse events	4			
occurence 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: • 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