Clinical trial results:
The effect of clinical characterization of children with monosymptomatic nocturnal enuresis on the efficacy of desmopressin and alarm therapy.

Summary

EudraCT number	2017-002169-23
Trial protocol	DK BE PL
Global end of trial date	03 January 2023

Results information

Result version number	v1 (current)
This version publication date	20 July 2023
First version publication date	20 July 2023

Trial information

Trial identification

Sponsor protocol code	DRYCHILD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03389412
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Cecilie Siggaard Jørgensen, MD, PhD, Aarhus University Hospital , cecisi@rm.dk
Scientific contact	Professor Søren Rittig, DMSc, Aarhus University Hospital , rittig@clin.au.dk

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	02 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2023
Global end of trial reached?	Yes
Global end of trial date	03 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate the importance of clinical characterization of children with monosymptomatic nocturnal enuresis in order to improve treatment efficacy.
Our hypothesis is that clinical characterization by measurement of nocturnal urine production and maximal voided volumes in children with monosymptomatic nocturnal enuresis and subsequent treatment tailoring improves the response to first-line treatment approach (desmopressin and alarm treatment).

Protection of trial subjects:

Once the informed consent form was signed, a unique patient number were assigned to each participant. In the final publication, data is handled as anonymous.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2017
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	China: 100
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Belgium: 46
Country: Number of subjects enrolled	Denmark: 171
Worldwide total number of subjects	324
EEA total number of subjects	224

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)	306
Adolescents (12-17 years)	18
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Most children Denmark were recruited from outside the hospital by posts on social media and newspaper advertisements. Children from Belgium and Poland were recruited from outpatient clinics, and a few children from Belgium were recruited from local schools. Children from China were recruited from outpatient clinics but without referral.

Pre-assignment

Screening details:

This was a medical assessment.

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Subject, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment based on prior consideration of voiding diaries

Arm description:

In this arm, treatment choice was based on voiding diaries. Children with nocturnal polyuria and normal maximum voided volume (MVV) received desmopressin treatment and children with reduced MVV and no nocturnal polyuria received an enuresis alarm.

Arm type	Experimental
Investigational medicinal product name	Desmopressin
Investigational medicinal product code	H01BA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oromucosal use

Dosage and administration details:

The children were treated with 120 microgram/day the first two weeks. If the child was not completely dry (revaluated by the parents), the dose were increased to 240 microgram / day the rest of the study period (maximum eight weeks of treatment). The tablet was administrated one hour before bedtime.

Arm title	Random allocation of treatment

Arm description:

In this arm, treatment with desmopressin or alarm was randomly allocated.

Arm type	Active comparator
Investigational medicinal product name	Desmopressin
Investigational medicinal product code	H01BA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oromucosal use

Dosage and administration details:

The children were treated with 120 microgram/day the first two weeks. If the child was not completely dry (revaluated by the parents), the dose were increased to 240 microgram / day the rest of the study period (maximum eight weeks of treatment). The tablet was administrated one hour before bedtime.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: Investigator was not blind in the study.

Number of subjects in period 1	Treatment based on prior consideration of voiding diaries	Random allocation of treatment
Started	161	163
Completed voiding diaries	150	149
Completed	141	140
Not completed	20	23
Did not complete voiding diaries	11	14
Developed daytime symptoms	1	1
Adherence to treatment <80%	8	8

Baseline characteristics

Reporting groups

Reporting group title	Treatment based on prior consideration of voiding diaries

Reporting group description:

In this arm, treatment choice was based on voiding diaries. Children with nocturnal polyuria and normal maximum voided volume (MVV) received desmopressin treatment and children with reduced MVV and no nocturnal polyuria received an enuresis alarm.

Reporting group title	Random allocation of treatment

Reporting group description:

In this arm, treatment with desmopressin or alarm was randomly allocated.

Reporting group values	Treatment based on prior consideration of voiding diaries	Random allocation of treatment	Total
Number of subjects	161	163	324
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	152	154	306
Adolescents (12-17 years)	9	9	18
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	8.1	8.1	
standard deviation	± 1.8	± 1.8	-
Gender categorical Units: Subjects			
Female	38	54	92
Male	123	109	232
Body mass index (BMI) Units: kg/m2			
arithmetic mean	16.4	16.9	
standard deviation	± 2.7	± 2.8	-

End points

End points reporting groups

Reporting group title	Treatment based on prior consideration of voiding diaries
Reporting group description:	
In this arm, treatment choice was based on voiding diaries. Children with nocturnal polyuria and normal maximum voided volume (MVV) received desmopressin treatment and children with reduced MVV and no nocturnal polyuria received an enuresis alarm.	
Reporting group title	Random allocation of treatment
Reporting group description:	
In this arm, treatment with desmopressin or alarm was randomly allocated.	

Primary: The number of children who responded to the treatment

End point title	The number of children who responded to the treatment
End point description:	
Defined by the International Children's Continence Society as a ≥ 50% reduction in number of wet nights per week and based on voiding diaries.	
End point type	Primary
End point timeframe:	
Measured at the end of treatment.	

End point values	Treatment based on prior consideration of voiding diaries	Random allocation of treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	140		
Units: Number of children	104	85		

Statistical analyses

Statistical analysis title	Generalized linear regression model
Statistical analysis description:	
Generalized linear regression model with log link function that adjusted the standard errors for the center as clusters.	
Comparison groups	Treatment based on prior consideration of voiding diaries v Random allocation of treatment
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)

Confidence interval	
level	95 %
sides	2-sided

Primary: The number of children achieving complete dryness (complete responders)

End point title	The number of children achieving complete dryness (complete responders)

End point description:

End point type	Primary

End point timeframe:

Measured at the end of treatment.

End point values	Treatment based on prior consideration of voiding diaries	Random allocation of treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	140		
Units: Number of children	72	59		

Statistical analyses

Statistical analysis title	Generalized linear regression model

Statistical analysis description:

Generalized linear regression model with log link function that adjusted the standard errors for the center as clusters.

Comparison groups	Random allocation of treatment v Treatment based on prior consideration of voiding diaries
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Risk ratio (RR)
Confidence interval	
level	95 %
sides	2-sided

Secondary: The reduction in wet nights

End point title	The reduction in wet nights

End point description:

End point type	Secondary

End point timeframe:

Measured at the end of treatment.

End point values	Treatment based on prior consideration of voiding diaries	Random allocation of treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	140		
Units: Wet nights/week				
arithmetic mean (standard deviation)	4.1 (± 2.7)	3.4 (± 2.8)		

Statistical analyses

Statistical analysis title	Mixed model with center as random effect
Comparison groups	Treatment based on prior consideration of voiding diaries v Random allocation of treatment
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events and reaction were reported between the first dose administration of trial medication / start of alarm treatment and the last trial related activity.

Adverse event reporting additional description:

Events occurring within a period of 30 days following the last intake of trial medication were also handled as such if spontaneously reported to the investigator.
At all clinical visits, the children and parents were asked about adverse events and reactions, and the families were at all-time able to contact the investigators to report any.

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	Subjects treated with Desmopressin
Reporting group description: -	
Reporting group title	Subjects treated with an enuresis alarm

Reporting group description: -

Serious adverse events	Subjects treated with Desmopressin	Subjects treated with an enuresis alarm	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 146 (0.68%)	0 / 155 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Urinary tract infection bacterial	Additional description: Hospitalisation		
subjects affected / exposed	1 / 146 (0.68%)	0 / 155 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Subjects treated with Desmopressin	Subjects treated with an enuresis alarm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 146 (1.37%)	6 / 155 (3.87%)	
Cardiac disorders			

Coarctation of the aorta	Additional description: No relation to the study, but was discovered during the study period.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 146 (0.00%)	1 / 155 (0.65%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 146 (1.37%)	1 / 155 (0.65%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Rash	Additional description: Rash along the cord		
subjects affected / exposed	0 / 146 (0.00%)	1 / 155 (0.65%)	
occurrences (all)	0	1	
Infections and infestations			
Cold and fever			
subjects affected / exposed	0 / 146 (0.00%)	2 / 155 (1.29%)	
occurrences (all)	0	2	
Product issues			
Entangled in the wire			
subjects affected / exposed	0 / 146 (0.00%)	1 / 155 (0.65%)	
occurrences (all)	0	0	

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