Clinical trial results:
A Double-blind, Randomised, Parallel-group Trial Investigating Sleep Behaviour and Daytime Performance in Nocturia Patients Treated with Desmopressin Orally Disintegrating Tablets as compared to Placebo.

Summary

EudraCT number	2012-004388-34
Trial protocol	GB
Global end of trial date	01 June 2014

Results information

Result version number	v1 (current)
This version publication date	01 March 2016
First version publication date	18 July 2015

Trial information

Trial identification

Sponsor protocol code	000088

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01779466
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	Kay Fiskers Plads 11, Copenhagen S, Denmark, 2300
Public contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@ferring.com
Scientific contact	Clinical Development Support, Ferring Pharmaceuticals, DK0-Disclosure@ferring.com

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	08 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2014
Global end of trial reached?	Yes
Global end of trial date	01 June 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Efficacy Objectives
• To investigate the relationship between nocturia, sleep, and daytime performance
• To investigate the efficacy of desmopressin orally disintegrating tablets (50 µg in men and 25 µg in women) versus placebo for treatment of patients with nocturia with respect to nocturia, sleep, and daytime performance.

Safety Objective
• To confirm the safety of desmopressin orally disintegrating tablets (50 µg in men and 25 µg in women) in the treatment of nocturia.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial including the possibility to discontinue at any time in language and terms appropriate for the patient and considering the local culture. Collected personal data and human biological samples were processed in compliance with the Declaration of Helsinki and its amendments in force at the initiation of the trial in compliance with the approved protocol and its amendments, Good Clinical Practice (GCP) and applicable regulatory requirements.

For safety reasons, serum sodium levels were monitored at regular intervals and a patient was to be withdrawn from the trial if the serum sodium level was ≤125 mmol/L or had any other sign of fluid overload such as peripheral or pulmonary oedema at any time point during the trial.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	09 April 2013
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	United Kingdom: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in United Kingdom between 09 Apr 2013 to 01 Jun 2014. Screening was stopped on 26 Feb 2014 due to poor recruitment. At that time, only five female subjects had been randomised.

Pre-assignment

Screening details:

The intent was to randomise eligible subjects to one of the three treatments: Placebo, Desmopressin 50 µg (for men), and Desmopressin 25 µg (for females). However, only five female subjects (three in Desmopressin 25 µg, two in Placebo) and no male subjects (Desmopressin 50 µg) could be enrolled in the trial.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

Treatment was blinded throughout. Both active and placebo IMP were provided as round, white tablets, marked with a diamond shaped figure on one side.

Arms

Are arms mutually exclusive?	Yes
Arm title	Desmopressin 25 µg orally disintegrating tablets

Arm description:

Desmopressin 25 µg orally disintegrating tablets for sublingual administration in the strength of 25 µg – for women only

Arm type	Experimental
Investigational medicinal product name	Desmopressin 25 µg
Investigational medicinal product code	FE 992026
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

Subjects had to take one orally disintegrating tablet each night, approximately one hour prior to bedtime, for the entire duration of the three-month treatment period. Patients were instructed to place the tablet under the tongue and not to chew or swallow the table. They were also advised to minimise fluid intake from two hours before bedtime until seven hours after.

Arm title	Placebo

Arm description:

Placebo (not active) orally disintegrating tablets for sublingual administration – for both men and women.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

Patients had to take one orally disintegrating tablet each night, approximately one hour prior to bedtime, for the entire duration of the three-month treatment period. Patients were instructed to place

the tablet under the tongue and not to chew or swallow the table. They were also advised to minimise fluid intake from two hours before bedtime until seven hours after.

Number of subjects in period 1	Desmopressin 25 µg orally disintegrating tablets	Placebo
Started	3	2
Completed	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	5	5	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	5	
Male	0	0	

End points

End points reporting groups

Reporting group title	Desmopressin 25 µg orally disintegrating tablets
Reporting group description:	
Desmopressin 25 µg orally disintegrating tablets for sublingual administration in the strength of 25 µg – for women only	
Reporting group title	Placebo
Reporting group description:	
Placebo (not active) orally disintegrating tablets for sublingual administration – for both men and women.	

Primary: Efficacy Endpoints

End point title	Efficacy Endpoints[1]
End point description:	
There was no efficacy evaluation.	
End point type	Primary
End point timeframe:	
There was no efficacy evaluation.	

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 efficacy objectives/endpoints were analysed due to low number of subjects.

End point values	Desmopressin 25 µg orally disintegrating tablets	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Nocturia/Sleep/Daytime endpoints				

Notes:

[2] - Efficacy not evaluated since only five females were enrolled.

[3] - Efficacy not evaluated since only five females were enrolled.

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant laboratory results

End point title	Clinically significant laboratory results[4]
End point description:	
Safety laboratory variables included clinical chemistry, haematology and urinalysis. The Investigator reviewed the laboratory results and documented whether the results were normal or abnormal, and whether results were clinically or not clinically significant.	
End point type	Primary
End point timeframe:	
Blood and urine samples for the assessment of safety laboratory variables were taken at Visit 0 (Screening) and Visit 5, Day 3. An additional blood sample for the analysis and monitoring of serum sodium were taken at Visit 3.	

Notes:

[4] - 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: The safety assessments were only presented as patient data listings i.e., no statistical analyses was performed as only five female subjects were enrolled in the trial.

End point values	Desmopressin 25 µg orally disintegrating tablets	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Number of subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically significant vital signs and physical examinations

End point title	Clinically significant vital signs and physical examinations[5]

End point description:

Vitals: Diastolic and systolic blood pressure (mmHg) and pulse (beats per minute) were measured after resting for 5 minutes in a sitting position. Vital signs measurements outside normal ranges were to be assessed as "abnormal, not clinically significant" or "abnormal, clinically significant" by the Investigator. Any abnormal, clinically significant changes were to be reported as adverse events (AEs).
Physical examinations: Physical examinations were performed by the Investigator or a delegated medically licensed qualified Sub-investigator. Any abnormal, clinically significant changes was to be reported as AEs.

End point type	Primary

End point timeframe:

Vitals (Blood pressure and pulse rate): Visit 0, each day of Visits 2, 3, 4 and 5.
Physical examinations:Visit 0 and Visit 5; Day 3.

Notes:

[5] - 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: The safety assessments were only presented as patient data listings i.e., no statistical analyses was performed as only five female subjects were enrolled in the trial.

End point values	Desmopressin 25 µg orally disintegrating tablets	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Number of subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Investigator monitored the condition of the patient throughout the trial from the time of obtaining informed consent until the last visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Desmopressin 25 µg orally disintegrating tablets

Reporting group description:

AEs are presented by-subject for one of the three subjects dosed with Desmopressin 25 µg orally disintegrating tablets.

Reporting group title	Placebo

Reporting group description:

AEs are presented by-subject for one of the two subjects dosed with placebo orally disintegrating tablets.

Serious adverse events	Desmopressin 25 µg orally disintegrating tablets	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Desmopressin 25 µg orally disintegrating tablets	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	2 / 2 (100.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 3 (66.67%)	2 / 2 (100.00%)	
occurrences (all)	5	8	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 3 (0.00%)	2 / 2 (100.00%)	
occurrences (all)	0	2	
Thirst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Skin irritation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 2 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 2 (50.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2013	Inclusion criteria updated to: •Male or female patients, aged 25-65 years (in place of 35-65 years) at the time of written consent, who currently had a regular sleep/wake schedule with minimal daytime napping (in place of a regular daytime schedule) •At least 2 nocturnal voids per night as judged by the Investigator during both 3-day diary periods •A habitual time-in-bed period, attempting to sleep, of between 6.0 and 9.5 hours per night (based on screening diary [CSD] and actigraphy) The exclusion criteria regarding stress incontinence was updated to only moderate or severe cases, as judged by the Investigator.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 February 2014	Due to poor recruitment the recruitment of patients in this trial was stopped on 20th of Feb 2014, with only five female patients randomised.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The trial also included a third arm Desmopressin 50 µg orally disintegrating tablets for sublingual administration, for men only. However, no subjects could be enrolled in the arm, hence the details are not presented.

Notes: