Clinical trial results:
A Randomised, Double-blind, Placebo-controlled, Response-adaptive Dose-finding Trial Investigating the Efficacy, Safety and Tolerability of Oral Doses of FE 201836, with Desmopressin Orally Disintegrating Tablet as a Benchmark, During 12 Weeks of Treatment for Nocturia due to Nocturnal Polyuria in Adults

Summary

EudraCT number	2016-003851-31
Trial protocol	CZ HU BE
Global end of trial date	31 October 2019

Results information

Result version number	v1 (current)
This version publication date	13 November 2020
First version publication date	13 November 2020

Trial information

Trial identification

Sponsor protocol code	000233

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03201419
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	International PharmaScience Center, Kay Fiskers Plads 11, Copenhagen S, Denmark, 2300
Public contact	Global Clinical Compliance, Ferring pharmaceuticals, DK0-Disclosure@ferring.com
Scientific contact	Global Clinical Compliance, 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	12 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2019
Global end of trial reached?	Yes
Global end of trial date	31 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the dose-response of FE 201836 with respect to the number of nocturnal voids in subjects with nocturia due to nocturnal polyuria.

Protection of trial subjects:

The trial was performed in accordance with the Declaration of Helsinki and its amendments in force at the initiation of the trial, the consolidated International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use-Good Clinical Practice (ICH-GCP), the European Union (EU) Clinical Trials Directive, and applicable national laws in the countries where the trial was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 64
Country: Number of subjects enrolled	United States: 420
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 32
Country: Number of subjects enrolled	Hungary: 11
Worldwide total number of subjects	531
EEA total number of subjects	47

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)	330
From 65 to 84 years	198
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

A total of 71 sites were authorised to recruit subjects for the trial between July 2017 and July 2019. The trial sites that screened subjects to the trial were: 5 in Belgium, 10 in Canada, 5 in Czech Republic, 2 in Germany, 5 in Hungary, 1 in Poland and 43 in the United States of America (USA).

Pre-assignment

Screening details:

A total of 1721 subjects were screened, wherein, 531 met the eligibility criteria and entered the enrichment period. Of these, 302 subjects met the eligibility criteria at Visit (V) 4 (randomisation), and were randomised to treatment with FE 201836 (different doses), placebo, or desmopressin. A total of 278 subjects completed the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FE 201836 500 µg (Randomised Treatment Period)

Arm description:

FE 201836 500 µg oral solution and placebo orally disintegrating tablet (ODT)

Arm type	Experimental
Investigational medicinal product name	FE 201836 500 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 500 µg oral solution and placebo ODT, administered once daily

Arm title	FE 201836 350 µg (Randomised Treatment Period)

Arm description:

FE 201836 350 µg oral solution and placebo ODT

Arm type	Experimental
Investigational medicinal product name	FE 201836 350 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 350 µg oral solution and placebo ODT, administered once daily

Arm title	FE 201836 250 µg (Randomised Treatment Period)

Arm description:

FE 201836 250 µg oral solution and placebo ODT

Arm type	Experimental

Investigational medicinal product name	FE 201836 250 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 250 µg oral solution and placebo ODT, administered once daily

Arm title	FE 201836 150 µg (Randomised Treatment Period)

Arm description:

FE 201836 150 µg oral solution and placebo ODT

Arm type	Experimental
Investigational medicinal product name	FE 201836 150 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 150 µg oral solution and placebo ODT, administered once daily

Arm title	FE 201836 100 µg (Randomised Treatment Period)

Arm description:

FE 201836 100 µg oral solution and placebo ODT

Arm type	Experimental
Investigational medicinal product name	FE 201836 100 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 100 µg oral solution and placebo ODT, administered once daily

Arm title	FE 201836 50 µg (Randomised Treatment Period)

Arm description:

FE 201836 50 µg oral solution and placebo ODT

Arm type	Experimental
Investigational medicinal product name	FE 201836 50 µg
Investigational medicinal product code	FE 201836
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

FE 201836 50 µg oral solution and placebo ODT, administered once daily

Arm title	Placebo (Randomised Treatment Period)

Arm description:

Placebo oral solution and placebo ODT

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution, Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo oral solution and placebo ODT, administered once daily

Arm title	Desmopressin 25 µg (Randomised Treatment Period)

Arm description:

Desmopressin 25 µg ODT and placebo oral solution

Arm type	Active comparator
Investigational medicinal product name	Desmopressin 25 µg (Randomised Treatment Period)
Investigational medicinal product code	
Other name	NOCDURNA
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Desmopressin 25 µg ODT and placebo oral solution, administered once daily (female subjects)

Arm title	Desmopressin 50 µg (Randomised Treatment Period)

Arm description:

Desmopressin 50 µg ODT and placebo oral solution

Arm type	Active comparator
Investigational medicinal product name	Desmopressin 50 µg (Randomised Treatment Period)
Investigational medicinal product code	
Other name	NOCDURNA
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Desmopressin 50 µg ODT and placebo oral solution, administered once daily (male subjects)

Number of subjects in period 1[1]	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)
Started	60	27	24
Completed	52	24	22
Not completed	8	3	2
Consent withdrawn by subject	4	2	1
Adverse event, non-fatal	3	1	-
Other	-	-	1
Lost to follow-up	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1[1]	FE 201836 150 µg (Randomised Treatment Period)	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)
Started	14	13	34
Completed	14	12	33
Not completed	0	1	1

Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	1	1
Other	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Placebo (Randomised Treatment Period)	Desmopressin 25 µg (Randomised Treatment Period)	Desmopressin 50 µg (Randomised Treatment Period)
Started	87	26	17
Completed	81	25	15
Not completed	6	1	2
Consent withdrawn by subject	-	1	2
Adverse event, non-fatal	5	-	-
Other	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	1	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 531 subjects met eligibility criteria and entered enrichment period (including active run-in period and washout period). During active run-in period subjects received FE 201836 500 µg and placebo to assess safety and establish subjects who respond to treatment with FE 201836 for inclusion in the trial (enrichment design). Of these, 302 subjects met eligibility criteria at V4 (randomisation), and were randomised to treatment with FE 201836 (different doses), placebo and desmopressin.

Baseline characteristics

Reporting groups	
Reporting group title	FE 201836 500 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 500 µg oral solution and placebo orally disintegrating tablet (ODT)	
Reporting group title	FE 201836 350 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 350 µg oral solution and placebo ODT	
Reporting group title	FE 201836 250 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 250 µg oral solution and placebo ODT	
Reporting group title	FE 201836 150 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 150 µg oral solution and placebo ODT	
Reporting group title	FE 201836 100 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 100 µg oral solution and placebo ODT	
Reporting group title	FE 201836 50 µg (Randomised Treatment Period)
Reporting group description:	
FE 201836 50 µg oral solution and placebo ODT	
Reporting group title	Placebo (Randomised Treatment Period)
Reporting group description:	
Placebo oral solution and placebo ODT	
Reporting group title	Desmopressin 25 µg (Randomised Treatment Period)
Reporting group description:	
Desmopressin 25 µg ODT and placebo oral solution	
Reporting group title	Desmopressin 50 µg (Randomised Treatment Period)
Reporting group description:	
Desmopressin 50 µg ODT and placebo oral solution	

Reporting group values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)
Number of subjects	60	27	24
Age categorical Units: Subjects			
<65 years old	35	19	14
>=65 years old	25	8	10
Age continuous Units: years			
arithmetic mean	59.0	58.0	60.8
standard deviation	± 14.1	± 14.3	± 13.0
Gender categorical Units: Subjects			
Female	40	18	16
Male	20	9	8

Baseline body mass index (BMI)			
Units: kg/m^2			
arithmetic mean	30.66	29.91	29.56
standard deviation	± 6.05	± 4.64	± 6.50
Mean Number of Nocturnal Voids			
FE 201836 500 ug: n=59; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=299			
Units: nocturnal voids			
arithmetic mean	2.88	3.01	3.10
standard deviation	± 0.84	± 0.72	± 1.11
Mean Nocturnal Urine Volume (NUV)			
FE 201836 500 ug: n=58; FE 201836 350 ug: n=26; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: mL			
arithmetic mean	804.6	766.0	897.3
standard deviation	± 313.8	± 242.1	± 373.6
Mean Nocturnal Polyuria Index			
FE 201836 500 ug: n=55; FE 201836 350 ug: n=25; FE 201836 250 ug: n=22; FE 201836 100 ug: n=12; FE 201836 50 ug: n=31; Placebo: n=76; Desmopressin 25µg: n=23; Desmopressin 50 µg: n=16 Total: n=274			
Units: percentage			
arithmetic mean	48.87	46.76	49.75
standard deviation	± 12.04	± 10.08	± 15.96
Mean Nocturia Impact (NI) Diary Total Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	47.20	47.03	38.76
standard deviation	± 18.39	± 28.44	± 19.09
Mean NI Diary Overall Impact Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	59.2	62.3	55.9
standard deviation	± 25.4	± 29.8	± 21.6
Insomnia Severity Index (ISI)			
FE201836 500 ug: n=55; FE 201836 350 ug: n=26; FE 201836 100 ug: n=9; FE 201836 50 ug: n=31; Placebo: n=77 Total: n=279			
Units: score on a scale			
arithmetic mean	15.8	15.7	14.3
standard deviation	± 5.4	± 6.1	± 5.1

Reporting group values	FE 201836 150 µg (Randomised Treatment Period)	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)
Number of subjects	14	13	34
Age categorical			
Units: Subjects			
<65 years old	6	6	21
>=65 years old	8	7	13
Age continuous			
Units: years			
arithmetic mean	63.9	61.5	59.1

standard deviation	± 7.5	± 9.2	± 10.4

Gender categorical Units: Subjects			
Female	5	8	16
Male	9	5	18
Baseline body mass index (BMI) Units: kg/m^2			
arithmetic mean	32.03	31.52	30.93
standard deviation	± 8.26	± 4.60	± 6.16
Mean Number of Nocturnal Voids			
FE 201836 500 ug: n=59; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=299			
Units: nocturnal voids			
arithmetic mean	2.98	3.33	3.24
standard deviation	± 0.84	± 0.82	± 1.18
Mean Nocturnal Urine Volume (NUV)			
FE 201836 500 ug: n=58; FE 201836 350 ug: n=26; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: mL			
arithmetic mean	803.1	892.4	879.9
standard deviation	± 304.7	± 206.7	± 354.1
Mean Nocturnal Polyuria Index			
FE 201836 500 ug: n=55; FE 201836 350 ug: n=25; FE 201836 250 ug: n=22; FE 201836 100 ug: n=12; FE 201836 50 ug: n=31; Placebo: n=76; Desmopressin 25µg: n=23; Desmopressin 50 µg: n=16 Total: n=274			
Units: percentage			
arithmetic mean	50.99	44.59	47.01
standard deviation	± 12.93	± 6.58	± 9.86
Mean Nocturia Impact (NI) Diary Total Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	36.28	51.63	42.46
standard deviation	± 22.10	± 17.73	± 23.28
Mean NI Diary Overall Impact Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	53.0	68.6	59.9
standard deviation	± 30.6	± 20.7	± 26.8
Insomnia Severity Index (ISI)			
FE201836 500 ug: n=55; FE 201836 350 ug: n=26; FE 201836 100 ug: n=9; FE 201836 50 ug: n=31; Placebo: n=77 Total: n=279			
Units: score on a scale			
arithmetic mean	13.0	16.4	14.7
standard deviation	± 6.7	± 5.6	± 4.8

Reporting group values	Placebo (Randomised Treatment Period)	Desmopressin 25 µg (Randomised Treatment Period)	Desmopressin 50 µg (Randomised Treatment Period)
Number of subjects	87	26	17

Age categorical Units: Subjects			
<65 years old	52	24	11
>=65 years old	35	2	6
Age continuous Units: years			
arithmetic mean	58.9	51.1	60.9
standard deviation	± 13.9	± 11.1	± 9.5
Gender categorical Units: Subjects			
Female	51	26	0
Male	36	0	17
Baseline body mass index (BMI) Units: kg/m^2			
arithmetic mean	29.54	31.89	31.05
standard deviation	± 5.14	± 7.99	± 6.49
Mean Number of Nocturnal Voids			
FE 201836 500 ug: n=59; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=299			
Units: nocturnal voids			
arithmetic mean	3.09	3.38	3.16
standard deviation	± 0.83	± 1.45	± 1.22
Mean Nocturnal Urine Volume (NUV)			
FE 201836 500 ug: n=58; FE 201836 350 ug: n=26; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: mL			
arithmetic mean	752.3	839.3	803.5
standard deviation	± 269.5	± 286.4	± 425.8
Mean Nocturnal Polyuria Index			
FE 201836 500 ug: n=55; FE 201836 350 ug: n=25; FE 201836 250 ug: n=22; FE 201836 100 ug: n=12; FE 201836 50 ug: n=31; Placebo: n=76; Desmopressin 25µg: n=23; Desmopressin 50 µg: n=16 Total: n=274			
Units: percentage			
arithmetic mean	47.91	49.21	49.10
standard deviation	± 14.29	± 13.93	± 17.93
Mean Nocturia Impact (NI) Diary Total Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	47.66	58.06	39.88
standard deviation	± 21.25	± 20.78	± 23.08
Mean NI Diary Overall Impact Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	62.7	71.5	54.2
standard deviation	± 26.8	± 23.8	± 28.0
Insomnia Severity Index (ISI)			
FE201836 500 ug: n=55; FE 201836 350 ug: n=26; FE 201836 100 ug: n=9; FE 201836 50 ug: n=31; Placebo: n=77 Total: n=279			
Units: score on a scale			
arithmetic mean	15.6	18.2	15.5

standard deviation	± 5.8	± 4.7	± 6.8

Reporting group values	Total		
Number of subjects	302		
Age categorical Units: Subjects			
<65 years old	188		
>=65 years old	114		
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	180		
Male	122		
Baseline body mass index (BMI) Units: kg/m^2 arithmetic mean standard deviation	- -		
Mean Number of Nocturnal Voids			
FE 201836 500 ug: n=59; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=299			
Units: nocturnal voids arithmetic mean standard deviation	- -		
Mean Nocturnal Urine Volume (NUV)			
FE 201836 500 ug: n=58; FE 201836 350 ug: n=26; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: mL arithmetic mean standard deviation	- -		
Mean Nocturnal Polyuria Index			
FE 201836 500 ug: n=55; FE 201836 350 ug: n=25; FE 201836 250 ug: n=22; FE 201836 100 ug: n=12; FE 201836 50 ug: n=31; Placebo: n=76; Desmopressin 25µg: n=23; Desmopressin 50 µg: n=16 Total: n=274			
Units: percentage arithmetic mean standard deviation	- -		
Mean Nocturia Impact (NI) Diary Total Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale arithmetic mean standard deviation	- -		
Mean NI Diary Overall Impact Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale arithmetic mean			

standard deviation	-		
Insomnia Severity Index (ISI)			
FE201836 500 ug: n=55; FE 201836 350 ug: n=26; FE 201836 100 ug: n=9; FE 201836 50 ug: n=31; Placebo: n=77 Total: n=279			
Units: score on a scale			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	ITT-RT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT-RT comprised of all the subjects randomised at V4.

Reporting group values	ITT-RT		
Number of subjects	302		
Age categorical Units: Subjects			
<65 years old	188		
>=65 years old	114		
Age continuous Units: years			
arithmetic mean	58.8		
standard deviation	± 12.8		
Gender categorical Units: Subjects			
Female	180		
Male	122		
Baseline body mass index (BMI) Units: kg/m^2			
arithmetic mean	30.44		
standard deviation	± 6.00		
Mean Number of Nocturnal Voids			
FE 201836 500 ug: n=59; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=299			
Units: nocturnal voids			
arithmetic mean	3.09		
standard deviation	± 0.98		
Mean Nocturnal Urine Volume (NUV)			
FE 201836 500 ug: n=58; FE 201836 350 ug: n=26; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: mL			
arithmetic mean	808.8		
standard deviation	± 307.5		
Mean Nocturnal Polyuria Index			
FE 201836 500 ug: n=55; FE 201836 350 ug: n=25; FE 201836 250 ug: n=22; FE 201836 100 ug: n=12; FE 201836 50 ug: n=31; Placebo: n=76; Desmopressin 25µg: n=23; Desmopressin 50 µg: n=16 Total: n=274			
Units: percentage			
arithmetic mean	48.24		
standard deviation	± 12.99		

Mean Nocturia Impact (NI) Diary Total Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	46.30		
standard deviation	± 21.81		
Mean NI Diary Overall Impact Score			
FE 201836 350 ug: n=26; FE 201836 50 ug: n=32; Placebo: n=86; Desmopressin 25µg: n=25 Total: n=297			
Units: score on a scale			
arithmetic mean	61.2		
standard deviation	± 26.3		
Insomnia Severity Index (ISI)			
FE201836 500 ug: n=55; FE 201836 350 ug: n=26; FE 201836 100 ug: n=9; FE 201836 50 ug: n=31; Placebo: n=77 Total: n=279			
Units: score on a scale			
arithmetic mean	15.6		
standard deviation	± 5.6		

End points reporting groups

Reporting group title	FE 201836 500 µg (Randomised Treatment Period)
Reporting group description: FE 201836 500 µg oral solution and placebo orally disintegrating tablet (ODT)	
Reporting group title	FE 201836 350 µg (Randomised Treatment Period)
Reporting group description: FE 201836 350 µg oral solution and placebo ODT	
Reporting group title	FE 201836 250 µg (Randomised Treatment Period)
Reporting group description: FE 201836 250 µg oral solution and placebo ODT	
Reporting group title	FE 201836 150 µg (Randomised Treatment Period)
Reporting group description: FE 201836 150 µg oral solution and placebo ODT	
Reporting group title	FE 201836 100 µg (Randomised Treatment Period)
Reporting group description: FE 201836 100 µg oral solution and placebo ODT	
Reporting group title	FE 201836 50 µg (Randomised Treatment Period)
Reporting group description: FE 201836 50 µg oral solution and placebo ODT	
Reporting group title	Placebo (Randomised Treatment Period)
Reporting group description: Placebo oral solution and placebo ODT	
Reporting group title	Desmopressin 25 µg (Randomised Treatment Period)
Reporting group description: Desmopressin 25 µg ODT and placebo oral solution	
Reporting group title	Desmopressin 50 µg (Randomised Treatment Period)
Reporting group description: Desmopressin 50 µg ODT and placebo oral solution	
Subject analysis set title	ITT-RT
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT-RT comprised of all the subjects randomised at V4.	

Primary: Change From Baseline in Aggregated Mean Number of Nocturnal Voids During 12 Weeks of Treatment

End point title	Change From Baseline in Aggregated Mean Number of Nocturnal Voids During 12 Weeks of Treatment[1]

End point description:

Nocturnal voids were defined as voids occuring from 5 minutes after bedtime until rising in the morning.

The number of nocturnal voids at each visit was calculated as the average over the 3 consecutive 24 hour periods just prior to the respective visit. The visit-specific means were aggregated into a mean of current and preceding visits.

Level estimated for baseline value of mean number of nocturnal voids equal to 2 and 95% credibility interval (2.5 and 97.5 percentiles of the posterior distribution) instead of confidence interval are presented in this endpoint.

The analysis population included intention-to-treat analysis set for the randomised treatment period (ITT-RT) which comprised of all the subjects randomised at Visit 4.

End point type	Primary

End point timeframe:

Baseline, during 12 weeks of treatment

Notes:

[1] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. The primary analyses did not include data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	27	24	14
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.06 (-1.28 to -0.86)	-0.99 (-1.20 to -0.78)	-0.89 (-1.12 to -0.69)	-0.80 (-1.00 to -0.62)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	34	87	
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-0.77 (-0.97 to -0.59)	-0.76 (-0.95 to -0.58)	-0.76 (-0.95 to -0.58)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo

Statistical analysis description:

Based on a Bayesian analysis of a sigmoidal dose-response relationship.

Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.07

Statistical analysis title	FE 201836 350 ug, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.02

Statistical analysis title	FE 201836 250 ug, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0

Statistical analysis title	FE 201836 150 ug, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0

Statistical analysis title	FE 201836 100 ug, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0

Statistical analysis title	FE 201836 50 ug, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0

Secondary: Change From Baseline in Mean Number of Nocturnal Voids at Week 1

End point title	Change From Baseline in Mean Number of Nocturnal Voids at Week 1[2]

End point description:

Nocturnal voids were defined as voids occuring from 5 minutes after bedtime until rising in the morning.

The number of nocturnal voids at each visit was calculated as the average over the 3 consecutive 24 hour periods just prior to the respective visit.
Adjusted visit-specific mean changes from baseline in nocturnal voids are estimated using a baseline value of 2.
MMRM=Mixed Model for Repeated Measurements.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	24	24	14
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-0.714 (-1.005 to -0.424)	-1.162 (-1.577 to -0.747)	-0.722 (-1.149 to -0.296)	-0.520 (-1.058 to 0.017)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	33	80	
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-0.722 (-1.318 to -0.126)	-0.325 (-0.709 to 0.059)	-0.575 (-0.842 to -0.308)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4214 [3]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.139
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.201

Notes:

[3] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0101 [4]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.587
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.034
upper limit	-0.141

Notes:

[4] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5203 [5]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.148
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.599
upper limit	0.304

Notes:

[5] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8483 [6]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.055

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.508
upper limit	0.617

Notes:

[6] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6357 [7]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.147
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.759
upper limit	0.464

Notes:

[7] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2222 [8]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.152
upper limit	0.652

Notes:

[8] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Number of Nocturnal Voids at Week 4

End point title	Change From Baseline in Mean Number of Nocturnal Voids at Week 4[9]

End point description:

Nocturnal voids were defined as voids occuring from 5 minutes after bedtime until rising in the morning.

The number of nocturnal voids at each visit was calculated as the average over the 3 consecutive 24

hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[9] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	22	21	12
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.078 (-1.345 to -0.811)	-1.330 (-1.708 to -0.952)	-0.784 (-1.181 to -0.386)	-0.471 (-0.969 to 0.028)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	76	
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-0.952 (-1.469 to -0.435)	-0.518 (-0.866 to -0.171)	-0.912 (-1.152 to -0.673)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2909 [10]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.166

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.474
upper limit	0.143

Notes:

[10] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [11]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.418
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.824
upper limit	-0.011

Notes:

[11] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5438 [12]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.128
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.288
upper limit	0.545

Notes:

[12] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096 [13]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.441
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.079
upper limit	0.962

Notes:

[13] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8826 [14]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.568
upper limit	0.488

Notes:

[14] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0344 [15]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.394
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.029
upper limit	0.759

Notes:

[15] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Number of Nocturnal Voids at Week 8

End point title	Change From Baseline in Mean Number of Nocturnal Voids at Week 8[16]

End point description:

Nocturnal voids were defined as voids occuring from 5 minutes after bedtime until rising in the morning.

The number of nocturnal voids at each visit was calculated as the average over the 3 consecutive 24 hour periods just prior to the respective visit.
Adjusted visit-specific mean changes from baseline in nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[16] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	23	21	14
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.085 (-1.394 to -0.776)	-1.177 (-1.603 to -0.751)	-0.965 (-1.414 to -0.516)	-0.490 (-1.037 to 0.058)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	30	70	
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.077 (-1.671 to -0.484)	-0.786 (-1.187 to -0.386)	-0.953 (-1.233 to -0.672)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4732 [17]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.132
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.496
upper limit	0.231

Notes:

[17] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3394 [18]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.224
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.685
upper limit	0.237

Notes:

[18] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.96 [19]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.488
upper limit	0.463

Notes:

[19] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1131 [20]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.463
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.111
upper limit	1.037

Notes:

[20] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6853 [21]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.124
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.729
upper limit	0.48

Notes:

[21] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4364 [22]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.166
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.254
upper limit	0.587

Notes:

[22] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Number of Nocturnal Voids at Week 12

End point title	Change From Baseline in Mean Number of Nocturnal Voids at Week 12[23]

End point description:

Nocturnal voids were defined as voids occuring from 5 minutes after bedtime until rising in the morning.

The number of nocturnal voids at each visit was calculated as the average over the 3 consecutive 24 hour periods just prior to the respective visit.
Adjusted visit-specific mean changes from baseline in nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[23] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	19	19	14
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.256 (-1.568 to -0.944)	-1.120 (-1.558 to -0.683)	-0.850 (-1.301 to -0.400)	-0.674 (-1.206 to -0.142)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	29	69	
Units: nocturnal voids				
arithmetic mean (confidence interval 95%)	-1.053 (-1.650 to -0.456)	-0.921 (-1.317 to -0.524)	-0.957 (-1.237 to -0.677)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1106 [24]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.299
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.667
upper limit	0.069

Notes:

[24] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5005 [25]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.163
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.639
upper limit	0.313

Notes:

[25] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6604 [26]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	0.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.372
upper limit	0.586

Notes:

[26] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3178 [27]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	0.283
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.275
upper limit	0.842

Notes:

[27] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7561 [28]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.096
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.701
upper limit	0.51

Notes:

[28] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8614 [29]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	0.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.378
upper limit	0.452

Notes:

[29] - Threshold for significance at 0.05 level.

Secondary: Responder Rate in Nocturnal Voids at Week 1

End point title	Responder Rate in Nocturnal Voids at Week 1[30]

End point description:

Defined as 50% reduction in nocturnal voids from baseline.

Adjusted visit-specific estimated odds of at least 50% reduction mean number of nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 1

Notes:

[30] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	24	24	14
Units: odds for nocturnal voids				
arithmetic mean (confidence interval 95%)	0.844 (0.457 to 1.558)	1.202 (0.510 to 2.833)	0.682 (0.280 to 1.662)	0.818 (0.269 to 2.490)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	33	80	
Units: odds for nocturnal voids				
arithmetic mean (confidence interval 95%)	0.810 (0.240 to 2.738)	0.513 (0.227 to 1.157)	0.480 (0.272 to 0.848)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.117 [31]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.759
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.869
upper limit	3.56

Notes:

[31] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048 [32]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.505
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	6.214

Notes:

[32] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46 [33]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	3.602

Notes:

[33] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367 [34]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.704
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.535
upper limit	5.427

Notes:

[34] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.407 [35]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.689
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.489
upper limit	5.825

Notes:

[35] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.876 [36]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.069
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.462
upper limit	2.473

Notes:

[36] - Threshold for significance at 0.05 level.

Secondary: Responder Rate in Nocturnal Voids at Week 4

End point title	Responder Rate in Nocturnal Voids at Week 4[37]

End point description:

Defined as 50% reduction in nocturnal voids from baseline.

Adjusted visit-specific estimated odds of at least 50% reduction mean number of nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[37] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	22	21	12
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.199 (0.633 to 2.270)	5.851 (1.511 to 22.650)	0.634 (0.255 to 1.575)	0.534 (0.165 to 1.731)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	76	
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.760 (0.470 to 6.596)	0.683 (0.301 to 1.550)	1.235 (0.686 to 2.224)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.937 [38]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.971
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	2.005

Notes:

[38] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028 [39]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.738
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.183
upper limit	18.968

Notes:

[39] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166 [40]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.513
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.318

Notes:

[40] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174 [41]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.433
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.129
upper limit	1.447

Notes:

[41] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608 [42]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.425
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.369
upper limit	5.512

Notes:

[42] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.171 [43]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.553
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.237
upper limit	1.292

Notes:

[43] - Threshold for significance at 0.05 level.

Secondary: Responder Rate in Nocturnal Voids at Week 8

End point title	Responder Rate in Nocturnal Voids at Week 8[44]

End point description:

Defined as 50% reduction in nocturnal voids from baseline.

Adjusted visit-specific estimated odds of at least 50% reduction mean number of nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 8

Notes:

[44] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	23	21	14
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.395 (0.717 to 2.715)	3.398 (1.150 to 10.043)	1.928 (0.721 to 5.155)	0.877 (0.286 to 2.688)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	30	70	
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.039 (0.302 to 3.569)	1.489 (0.638 to 3.474)	1.503 (0.806 to 2.803)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.85 [45]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.928
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	2.003

Notes:

[45] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.15 [46]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.261
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.745
upper limit	6.862

Notes:

[46] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.632 [47]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.283
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.462
upper limit	3.566

Notes:

[47] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.363 [48]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.583
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.183
upper limit	1.863

Notes:

[48] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.555 [49]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.691
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.203
upper limit	2.359

Notes:

[49] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.984 [50]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.991
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.408
upper limit	2.405

Notes:

[50] - Threshold for significance at 0.05 level.

Secondary: Responder Rate in Nocturnal Voids at Week 12

End point title	Responder Rate in Nocturnal Voids at Week 12[51]

End point description:

Defined as 50% reduction in nocturnal voids from baseline.

Adjusted visit-specific estimated odds of at least 50% reduction mean number of nocturnal voids are estimated using a baseline value of 2.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[51] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	19	19	14
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	3.914 (1.830 to 8.370)	1.891 (0.693 to 5.163)	1.824 (0.694 to 4.795)	0.854 (0.279 to 2.611)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	29	69	
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.400 (0.401 to 4.893)	1.395 (0.611 to 3.181)	1.590 (0.844 to 2.993)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046 [52]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.462
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.017
upper limit	5.961

Notes:

[52] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745 [53]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.418
upper limit	3.386

Notes:

[53] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79 [54]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.147
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.417
upper limit	3.155

Notes:

[54] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293 [55]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.537
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.169
upper limit	1.71

Notes:

[55] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.843 [56]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.881
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.252
upper limit	3.076

Notes:

[56] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.763 [57]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.877
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.375
upper limit	2.053

Notes:

[57] - Threshold for significance at 0.05 level.

Secondary: Responder Rate in Nocturnal Voids During 12 Weeks of Treatment

End point title	Responder Rate in Nocturnal Voids During 12 Weeks of Treatment[58]

End point description:

Defined as 50% reduction in nocturnal voids from baseline.

Estimated odds of at least 50% reduction in the aggregated mean number of nocturnal voids for a subject with 2 nocturnal voids at baseline are presented in this endpoint.

The 95% credibility interval (2.5 and 97.5 percentiles of the posterior distribution) instead of confidence interval is presented for this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

During 12 weeks of treatment

Notes:

[58] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	27	24	14
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	1.129 (0.808 to 1.753)	1.095 (0.772 to 1.661)	1.032 (0.711 to 1.543)	0.934 (0.597 to 1.378)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	34	87	
Units: odds of nocturnal voids				
arithmetic mean (confidence interval 95%)	0.887 (0.555 to 1.253)	0.849 (0.534 to 1.187)	0.834 (0.514 to 1.180)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 500 µg (Randomised Treatment Period)
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.422
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.868
upper limit	2.597

Statistical analysis title	FE 201836 350 µg, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.373
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.905
upper limit	2.45

Statistical analysis title	FE 201836 250 µg, Placebo
Statistical analysis description: Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.284
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.927
upper limit	2.264

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.145
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.957
upper limit	1.896

Statistical analysis title	FE 201836 100 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.079
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.972
upper limit	1.638

Statistical analysis title	FE 201836 50 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.023

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.991
upper limit	1.313

Secondary: Change From Baseline in Mean NI Diary Total Score at Week 1

End point title	Change From Baseline in Mean NI Diary Total Score at Week

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall quality of life (QoL) impact question (Q12). The NI Diary Total Scores are calculated by summing the 11 core items. Responses are scored from 0 to 4 (lowest to highest impact). The NI Diary Total is standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit.
Adjusted visit-specific mean changes from baseline in NI Diary Total Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[59] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	23	24	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-7.55 (-11.67 to -3.43)	-21.91 (-28.15 to -15.68)	-10.90 (-17.17 to -4.63)	-8.93 (-17.15 to -0.72)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	83	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-9.68 (-18.41 to -0.94)	-8.75 (-14.27 to -3.23)	-8.07 (-11.48 to -4.65)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8463 [60]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.75
upper limit	5.78

Notes:

[60] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [61]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-13.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.89
upper limit	-6.81

Notes:

[61] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4355 [62]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-2.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.99
upper limit	4.32

Notes:

[62] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8483 [63]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.79
upper limit	8.06

Notes:

[63] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7336 [64]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.91
upper limit	7.69

Notes:

[64] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8347 [65]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.15
upper limit	5.78

Notes:

[65] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Total Score at Week 4

End point title	Change From Baseline in Mean NI Diary Total Score at Week

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). The NI Diary Total Scores are calculated by summing the 11 core items. Responses are scored from 0 to 4 (lowest to highest impact). The NI Diary Total is standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Total Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[66] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	24	22	13
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-12.62 (-16.89 to -8.35)	-17.44 (-23.80 to -11.08)	-14.37 (-20.96 to -7.78)	-11.23 (-19.82 to -2.65)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	31	78	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-22.23 (-31.11 to -13.35)	-13.29 (-19.00 to -7.58)	-14.20 (-17.77 to -10.64)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5695 [67]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	7.07

Notes:

[67] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3784 [68]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-3.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.46
upper limit	3.99

Notes:

[68] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9653 [69]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.67
upper limit	7.34

Notes:

[69] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5304 [70]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	2.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.35
upper limit	12.29

Notes:

[70] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0968 [71]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-8.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.51
upper limit	1.46

Notes:

[71] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7885 [72]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.79
upper limit	7.62

Notes:

[72] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Total Score at Week 8

End point title	Change From Baseline in Mean NI Diary Total Score at Week

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). The NI Diary Total Scores are calculated by summing the 11 core items. Responses are scored from 0 to 4 (lowest to highest impact). The NI Diary Total is standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit.
Adjusted visit-specific mean changes from baseline in NI Diary Total Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[73] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	24	23	14
Units: score on a scale				
arithmetic mean (confidence interval	-16.03 (-20.49	-23.22 (-29.79	-15.10 (-21.85	-12.04 (-20.77

95%)	to -11.57)	to -16.64)	to -8.35)	to -3.32)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	30	79	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-19.23 (-28.62 to -9.83)	-14.11 (-20.00 to -8.22)	-14.83 (-18.50 to -11.16)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6792 [74]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.89
upper limit	4.5

Notes:

[74] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0276 [75]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-8.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.84
upper limit	-0.93

Notes:
[75] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9445 [76]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.97
upper limit	7.42

Notes:
[76] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5637 [77]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	2.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.71
upper limit	12.28

Notes:
[77] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.387 [78]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-4.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.39
upper limit	5.6

Notes:

[78] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8373 [79]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.19
upper limit	7.63

Notes:

[79] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Total Score at Week 12

End point title	Change From Baseline in Mean NI Diary Total Score at Week

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). The NI Diary Total Scores are calculated by summing the 11 core items. Responses are scored from 0 to 4 (lowest to highest impact). The NI Diary Total is standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Total Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[80] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	22	21	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-16.92 (-21.66 to -12.18)	-24.44 (-31.52 to -17.35)	-14.68 (-21.94 to -7.42)	-10.13 (-19.37 to -0.88)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	77	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-22.59 (-32.46 to -12.71)	-17.18 (-23.39 to -10.96)	-17.45 (-21.36 to -13.53)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8646 [81]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.54
upper limit	6.59

Notes:

[81] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087 [82]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-6.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	1.02

Notes:

[82] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51 [83]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	11.04

Notes:

[83] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1535 [84]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	7.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.75
upper limit	17.39

Notes:

[84] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3369 [85]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-5.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.66
upper limit	5.38

Notes:

[85] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9417 [86]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.05
upper limit	7.59

Notes:

[86] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Aggregated Mean NI Diary Total Score During 12 Weeks of Treatment

End point title	Change From Baseline in Aggregated Mean NI Diary Total Score During 12 Weeks of Treatment[87]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). The NI Diary Total Scores are calculated by summing the 11 core items. Responses are scored from 0 to 4 (lowest to highest impact). The NI Diary Total is standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the mean over the three consecutive 24 hour periods just prior to the respective visit. The visit-specific means were aggregated into a mean of current and preceding visits.

Level estimated for baseline value of mean NI Diary Total Score equal to 40 is presented in this endpoint.

The 95% credibility interval (2.5 and 97.5 percentiles of the posterior distribution) instead of confidence interval is presented for this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, during 12 weeks of treatment

Notes:

[87] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	27	24	14
Units: score on a scale				
median (confidence interval 95%)	-12.40 (-14.71 to -8.59)	-12.69 (-15.07 to -10.53)	-12.75 (-15.16 to -10.57)	-12.77 (-15.21 to -10.59)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	34	87	
Units: score on a scale				
median (confidence interval 95%)	-12.77 (-15.23 to -10.54)	-12.78 (-15.18 to -10.50)	-12.77 (-15.18 to -10.47)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo

Statistical analysis description:

Based on a Bayesian analysis of a sigmoidal dose-response relationship.

Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	5.47

Statistical analysis title	FE 201836 350 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	1.19

Statistical analysis title	FE 201836 250 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.5

Statistical analysis title	FE 201836 150 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.15

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.05

Statistical analysis title	FE 201836 50 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.01

Secondary: Percentage of Nights With at Most One Nocturnal Void During 12 Weeks of Treatment

End point title	Percentage of Nights With at Most One Nocturnal Void During 12 Weeks of Treatment[88]

End point description:

The percentages of nights during the treatment period with at most one nocturnal void are presented in this endpoint.

Level estimated for baseline value of mean number of nocturnal voids equal to 2 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

During 12 weeks of treatment

Notes:

[88] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	27	24	14
Units: percentage of nights				
arithmetic mean (confidence interval 95%)	67.2 (58.2 to 76.2)	77.5 (64.9 to 90.2)	64.5 (51.0 to 78.0)	55.3 (38.3 to 72.3)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	33	84	
Units: percentage of nights				
arithmetic mean (confidence interval 95%)	73.2 (55.1 to 91.2)	61.4 (49.3 to 73.5)	62.0 (53.8 to 70.2)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3328 [89]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	15.7

Notes:

[89] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0255 [90]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	29.2

Notes:

[90] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7296 [91]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	16.7

Notes:

[91] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4586 [92]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	-6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.5
upper limit	11.1

Notes:

[92] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2327 [93]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	29.5

Notes:

[93] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.924 [94]
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	12.1

Notes:

[94] - Threshold for significance at 0.05 level.

Secondary: Percentage of Nights With No Nocturnal Voids During 12 Weeks of Treatment

End point title	Percentage of Nights With No Nocturnal Voids During 12 Weeks of Treatment[95]

End point description:

The percentages of nights during the treatment period with complete response, i.e. no nocturnal voids are presented in this endpoint.

Level estimated for baseline value of mean number of nocturnal voids equal to 2 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

During 12 weeks of treatment

Notes:

[95] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	27	24	14
Units: percentage of nights				
arithmetic mean (confidence interval 95%)	23.3 (16.3 to 30.3)	28.8 (19.0 to 38.6)	17.3 (6.8 to 27.8)	12.9 (-0.3 to 26.1)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	33	84	
Units: percentage of nights				
arithmetic mean (confidence interval 95%)	14.8 (0.8 to 28.8)	21.5 (12.1 to 30.9)	23.0 (16.6 to 29.4)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 500 µg (Randomised Treatment Period)

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9499 [96]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	8.5

Notes:

[96] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2842 [97]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	16.4

Notes:

[97] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31 [98]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	-5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.8
upper limit	5.4

Notes:

[98] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1499 [99]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	-10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	3.7

Notes:

[99] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2571 [100]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	-8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.5
upper limit	6

Notes:

[100] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7629 [101]
Method	ANCOVA
Parameter estimate	Mean difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	8.3

Notes:

[101] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Overall Impact Score at Week 1

End point title	Change From Baseline in Mean NI Diary Overall Impact Score at Week 1[102]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). For the overall impact question (Q12), response options range from 0 (not at all) to 4 (a great deal). The NI Diary Overall Impact Scores are standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Overall Impact Score are estimated using a baseline value of 40

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[102] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	23	24	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-10.98 (-16.40 to -5.56)	-30.39 (-38.62 to -22.17)	-15.51 (-23.85 to -7.17)	-11.77 (-22.69 to -0.85)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	83	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-2.79 (-14.29 to 8.70)	-12.26 (-19.57 to -4.95)	-13.46 (-17.89 to -9.03)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4846 [103]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	9.46

Notes:

[103] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004 [104]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-16.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.26
upper limit	-7.6

Notes:

[104] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6685 [105]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.47
upper limit	7.37

Notes:
[105] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7772 [106]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.07
upper limit	13.46

Notes:
[106] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0895 [107]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	10.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	23

Notes:
[107] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.782 [108]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.34
upper limit	9.74

Notes:

[108] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Overall Impact Score at Week 4

End point title	Change From Baseline in Mean NI Diary Overall Impact Score at Week 4[109]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). For the overall impact question (Q12), response options range from 0 (not at all) to 4 (a great deal). The NI Diary Overall Impact Scores are standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Overall Impact Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[109] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	24	22	13
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-22.17 (-28.25 to -16.09)	-26.07 (-35.09 to -17.05)	-19.35 (-28.80 to -9.90)	-18.36 (-30.66 to -6.07)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	31	78	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-17.95 (-30.50 to -5.41)	-21.40 (-29.54 to -13.26)	-21.75 (-26.74 to -16.77)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9175 [110]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.25
upper limit	7.42

Notes:

[110] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4098 [111]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-4.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.62
upper limit	5.98

Notes:

[111] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6566 [112]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.25
upper limit	13.06

Notes:

[112] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6144 [113]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	3.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.85
upper limit	16.63

Notes:

[113] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5798 [114]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.71
upper limit	17.31

Notes:

[114] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9417 [115]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.17
upper limit	9.88

Notes:

[115] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Overall Impact Score at Week 8

End point title	Change From Baseline in Mean NI Diary Overall Impact Score at Week 8[116]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). For the overall impact question (Q12), response options range from 0 (not at all) to 4 (a great deal). The NI Diary Overall Impact Scores are standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Overall Impact Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[116] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	24	23	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-28.13 (-34.76 to -21.50)	-34.97 (-44.69 to -25.25)	-21.71 (-31.80 to -11.62)	-19.03 (-32.06 to -6.00)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	30	79	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-23.84 (-37.71 to -9.96)	-20.70 (-29.45 to -11.94)	-25.32 (-30.69 to -19.95)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5148 [117]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-2.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.31
upper limit	5.68

Notes:

[117] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0879 [118]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	-9.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.75
upper limit	1.44

Notes:

[118] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5335 [119]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.79
upper limit	15

Notes:

[119] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3787 [120]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	6.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.76
upper limit	20.34

Notes:

[120] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8448 [121]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.41
upper limit	16.38

Notes:

[121] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3751 [122]
Method	MMRM
Parameter estimate	Mean difference
Point estimate	4.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.63
upper limit	14.87

Notes:

[122] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NI Diary Overall Impact Score at Week 12

End point title	Change From Baseline in Mean NI Diary Overall Impact Score at Week 12[123]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). For the overall impact question (Q12), response options range from 0 (not at all) to 4 (a great deal). The NI Diary Overall Impact Scores are standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NI Diary Overall Impact Score are estimated using a baseline value of 40.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[123] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	22	21	14
Units: score on a scale				

arithmetic mean (confidence interval 95%)	-30.47 (-37.49 to -23.45)	-36.76 (-47.18 to -26.34)	-20.84 (-31.65 to -10.02)	-15.32 (-29.10 to -1.54)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	77	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-28.89 (-43.40 to -14.39)	-27.13 (-36.35 to -17.91)	-30.03 (-35.74 to -24.33)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9245 [124]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.43
upper limit	8.57

Notes:

[124] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2657 [125]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-6.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.59
upper limit	5.15

Notes:
[125] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1383 [126]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.99
upper limit	21.38

Notes:
[126] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0523 [127]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	14.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	29.59

Notes:
[127] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8855 [128]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	1.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.47
upper limit	16.75

Notes:

[128] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5972 [129]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.91
upper limit	13.72

Notes:

[129] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Aggregated Mean NI Diary Overall Impact Score During 12 Weeks of Treatment

End point title	Change From Baseline in Aggregated Mean NI Diary Overall Impact Score During 12 Weeks of Treatment[130]

End point description:

The NI Diary is a 12-item questionnaire with 11 core items (Q1-Q11) and an overall QoL impact question (Q12). For the overall impact question (Q12), response options range from 0 (not at all) to 4 (a great deal). The NI Diary Overall Impact Scores are standardised from 0 to 100 (lowest to highest impact).

The score at each visit was calculated as the average over the three consecutive 24 hour periods just prior to the respective visit. The visit-specific means were aggregated into a mean of current and preceding visits.

Level estimated for baseline value of mean NI Diary Overall Impact Score equal to 40 is presented in this endpoint.

The 95% credibility interval (2.5 and 97.5 percentiles of the posterior distribution) instead of confidence interval is presented for this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, during 12 weeks of treatment

Notes:

[130] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only.

None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	27	24	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-6.50 (-10.57 to -2.85)	-6.25 (-9.78 to -3.03)	-6.11 (-9.49 to -2.90)	-6.00 (-9.28 to -2.70)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	34	87	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-5.98 (-9.29 to -2.58)	-5.97 (-9.32 to -2.57)	-5.96 (-9.42 to -2.49)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.09
upper limit	2.28

Statistical analysis title	FE 201836 350 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg

	(Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	0.75

Statistical analysis title	FE 201836 250 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	0.33

Statistical analysis title	FE 201836 150 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.07

Statistical analysis title	FE 201836 100 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.02

Statistical analysis title	FE 201836 50 µg, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0

Secondary: Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 1

End point title	Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 1[131]

End point description:

The PGI-I is a 1-item questionnaire designed to assess the patient's impression of changes in urinary symptoms. The PGI-I was scored from 1 (very much better) to 7 (very much worse).

Visit-specific PGI-I in urinary symptoms is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 1

Notes:

[131] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	23	24	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	2.475 (2.261 to 2.689)	2.045 (1.723 to 2.367)	2.708 (2.385 to 3.031)	2.786 (2.363 to 3.209)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	33	81	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	2.781 (2.316 to 3.245)	2.758 (2.482 to 3.033)	2.745 (2.571 to 2.919)	

Statistical analyses

Statistical analysis title	FE 201836 500 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 500 µg (Randomised Treatment Period)
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055 [132]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.545
upper limit	0.006

Notes:

[132] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 µg, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [133]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.066
upper limit	-0.335

Notes:

[133] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.844 [134]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.404
upper limit	0.33

Notes:

[134] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.861 [135]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.417
upper limit	0.498

Notes:

[135] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8871 [136]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.532

Notes:

[136] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 µg, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9396 [137]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.313
upper limit	0.338

Notes:

[137] - Threshold for significance at 0.05 level.

Secondary: Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 4

End point title	Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 4[138]

End point description:

The PGI-I is a 1-item questionnaire designed to assess the patient's impression of changes in urinary symptoms. The PGI-I was scored from 1 (very much better) to 7 (very much worse).

Visit-specific PGI-I in urinary symptoms is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 4

Notes:

[138] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	24	20	12
Units: score on a scale				
arithmetic mean (confidence interval 95%)	2.121 (1.866 to 2.376)	2.191 (1.813 to 2.569)	2.447 (2.039 to 2.855)	2.521 (1.995 to 3.047)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	30	77	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	2.385 (1.859 to 2.910)	2.582 (2.244 to 2.921)	2.596 (2.386 to 2.806)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 500 µg (Randomised Treatment Period)
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [139]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.475
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.806
upper limit	-0.145

Notes:
[139] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0665 [140]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.405
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.837
upper limit	0.028

Notes:
[140] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5245 [141]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.149
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.608
upper limit	0.31

Notes:
[141] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7947 [142]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.075

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.642
upper limit	0.492

Notes:

[142] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4625 [143]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.211
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.777
upper limit	0.355

Notes:

[143] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9465 [144]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.014
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.412
upper limit	0.385

Notes:

[144] - Threshold for significance at 0.05 level.

Secondary: Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 8

End point title	Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 8[145]

End point description:

The PGI-I is a 1-item questionnaire designed to assess the patient's impression of changes in urinary symptoms. The PGI-I was scored from 1 (very much better) to 7 (very much worse).

Visit-specific PGI-I in urinary symptoms is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 8

Notes:

[145] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	24	21	14
Units: score on a scale				
arithmetic mean (confidence interval 95%)	1.843 (1.572 to 2.113)	1.887 (1.493 to 2.281)	2.528 (2.109 to 2.947)	2.286 (1.761 to 2.811)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	28	78	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	2.155 (1.587 to 2.723)	2.273 (1.917 to 2.629)	2.573 (2.355 to 2.791)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [146]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.078
upper limit	-0.383

Notes:

[146] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [147]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.686
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.137
upper limit	-0.236

Notes:

[147] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.852 [148]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.045
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.517
upper limit	0.427

Notes:

[148] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3205 [149]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.287
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.856
upper limit	0.281

Notes:

[149] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1769 [150]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.418
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.026
upper limit	0.19

Notes:

[150] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1584 [151]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.717
upper limit	0.118

Notes:

[151] - Threshold for significance at 0.05 level.

Secondary: Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 12

End point title	Patient Global Impression of Improvement (PGI-I) Urinary Symptoms Scores at Week 12[152]

End point description:

The PGI-I is a 1-item questionnaire designed to assess the patient's impression of changes in urinary symptoms. The PGI-I was scored from 1 (very much better) to 7 (very much worse).

Visit-specific PGI-I in urinary symptoms is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[152] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	23	18	13
Units: score on a scale				
arithmetic mean (confidence interval 95%)	1.667 (1.357 to 1.977)	1.671 (1.224 to 2.119)	2.656 (2.167 to 3.146)	2.452 (1.855 to 3.049)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	72	
Units: score on a scale				
arithmetic mean (confidence interval 95%)	1.678 (1.052 to 2.304)	2.384 (1.994 to 2.774)	2.490 (2.240 to 2.740)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [153]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.822
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	-0.424

Notes:

[153] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0019 [154]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.818
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.331
upper limit	-0.306

Notes:

[154] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.551 [155]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.167
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.383
upper limit	0.716

Notes:

[155] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9086 [156]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.685
upper limit	0.61

Notes:

[156] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0185 [157]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.812
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.486
upper limit	-0.138

Notes:

[157] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6537 [158]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.569
upper limit	0.357

Notes:

[158] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Patient Global Impression of Severity (PGI-S) Scores at Week 1

End point title	Change From Baseline in Patient Global Impression of Severity (PGI-S) Scores at Week 1[159]

End point description:

The PGI-S is a 1-item questionnaire designed to assess patient's impression of disease severity. The PGI-S was scored from 1 (none) to 4 (severe).

Change from baseline in visit-specific PGI-S is presented in this endpoint.

Level estimated for baseline value of PGI-S equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[159] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	23	24	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.739 (-0.927 to -0.552)	-0.970 (-1.253 to -0.688)	-0.811 (-1.094 to -0.529)	-0.643 (-1.012 to -0.273)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	28	80	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.417 (-0.840 to 0.007)	-0.719 (-0.984 to -0.454)	-0.593 (-0.746 to -0.440)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo

	(Randomised Treatment Period)
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235 [160]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.146
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.388
upper limit	0.096

Notes:

[160] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0215 [161]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.377
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.699
upper limit	-0.056

Notes:

[161] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1818 [162]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.218
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.103

Notes:
[162] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8063 [163]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.35

Notes:
[163] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4414 [164]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.176
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.274
upper limit	0.627

Notes:
[164] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4179 [165]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.126

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.432
upper limit	0.18

Notes:

[165] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in PGI-S Scores at Week 4

End point title	Change From Baseline in PGI-S Scores at Week 4[166]

End point description:

The PGI-S is a 1-item questionnaire designed to assess patient's impression of disease severity. The PGI-S was scored from 1 (none) to 4 (severe).
Change from baseline in visit-specific PGI-S is presented in this endpoint.

Level estimated for baseline value of PGI-S equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[166] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	23	20	12
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.837 (-1.015 to -0.659)	-1.025 (-1.292 to -0.758)	-0.798 (-1.081 to -0.516)	-0.749 (-1.115 to -0.383)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	27	75	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.656 (-1.033 to -0.278)	-0.936 (-1.189 to -0.684)	-0.898 (-1.045 to -0.750)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6042 [167]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.292

Notes:

[167] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4114 [168]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.432
upper limit	0.177

Notes:

[168] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5394 [169]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.099

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.219
upper limit	0.418

Notes:

[169] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459 [170]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.149
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.246
upper limit	0.544

Notes:

[170] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2397 [171]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.242
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.163
upper limit	0.647

Notes:

[171] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7954 [172]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.039
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.332
upper limit	0.254

Notes:

[172] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in PGI-S Scores at Week 8

End point title	Change From Baseline in PGI-S Scores at Week 8[173]

End point description:

The PGI-S is a 1-item questionnaire designed to assess patient's impression of disease severity. The PGI-S was scored from 1 (none) to 4 (severe).
Change from baseline in visit-specific PGI-S is presented in this endpoint.

Level estimated for baseline value of PGI-S equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[173] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	23	21	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.132 (-1.322 to -0.942)	-1.410 (-1.688 to -1.132)	-0.825 (-1.114 to -0.536)	-0.643 (-1.004 to -0.281)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	25	76	

Units: score on a scale				
least squares mean (confidence interval 95%)	-0.816 (-1.215 to -0.418)	-1.013 (-1.279 to -0.747)	-0.800 (-0.953 to -0.647)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0077 [174]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.332
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.576
upper limit	-0.089

Notes:

[174] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [175]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.927
upper limit	-0.293

Notes:

[175] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)

Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8778 [176]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.026
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.352
upper limit	0.301

Notes:

[176] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4309 [177]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.157
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.235
upper limit	0.549

Notes:

[177] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9392 [178]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.444
upper limit	0.411

Notes:

[178] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1734 [179]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.213
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.521
upper limit	0.094

Notes:

[179] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in PGI-S Scores at Week 12

End point title	Change From Baseline in PGI-S Scores at Week 12[180]

End point description:

The PGI-S is a 1-item questionnaire designed to assess patient's impression of disease severity. The PGI-S was scored from 1 (none) to 4 (severe).
Change from baseline in visit-specific PGI-S is presented in this endpoint.

Level estimated for baseline value of PGI-S equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[180] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	22	18	13
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.181 (-1.383 to -0.979)	-1.338 (-1.630 to -1.045)	-0.894 (-1.208 to -0.579)	-0.638 (-1.020 to -0.257)

End point values	FE 201836 100 µg (Randomised Treatment	FE 201836 50 µg (Randomised Treatment	Placebo (Randomised Treatment Period)	

	Period)	Period)		
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	27	70	
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.168 (-1.571 to -0.764)	-1.041 (-1.312 to -0.770)	-0.853 (-1.016 to -0.690)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0133 [181]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.328
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.587
upper limit	-0.069

Notes:

[181] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0048 [182]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.484
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.819
upper limit	-0.15

Notes:

[182] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8223 [183]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.395
upper limit	0.314

Notes:

[183] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3083 [184]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.215
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.63

Notes:

[184] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1556 [185]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.315
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.121

Notes:

[185] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2423 [186]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.188
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.504
upper limit	0.128

Notes:

[186] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Hsu 5-point Likert Bother Scale at Week 1

End point title	Change From Baseline in Hsu 5-point Likert Bother Scale at Week 1[187]

End point description:

The Hsu 5-point Likert Bother scale is a questionnaire designed to assess the subjective bothersomeness and functional disruptiveness of nocturia. The Hsu 5 point Likert Bother Scale was scored from 0 (not at all) to 4 (extremely).

Change from baseline in visit-specific Hsu Bother is presented in this endpoint.

Level estimated for baseline value of Hsu Bother equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[187] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	23	24	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.649 (-0.922 to -0.376)	-1.072 (-1.441 to -0.703)	-0.748 (-1.125 to -0.370)	-0.458 (-0.942 to 0.026)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	30	70	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.346 (-0.955 to 0.262)	-0.376 (-0.714 to -0.039)	-0.570 (-0.799 to -0.341)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6381 [188]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.079
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.409
upper limit	0.251

Notes:

[188] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0221 [189]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.502
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.931
upper limit	-0.073

Notes:

[189] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4112 [190]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.177
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.602
upper limit	0.247

Notes:

[190] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6761 [191]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.112
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.416
upper limit	0.64

Notes:

[191] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4898 [192]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.224
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.414
upper limit	0.861

Notes:

[192] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3311 [193]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.194
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.198
upper limit	0.585

Notes:

[193] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Hsu 5-point Likert Bother Scale at Week 4

End point title	Change From Baseline in Hsu 5-point Likert Bother Scale at Week 4[194]

End point description:

The Hsu 5-point Likert Bother scale is a questionnaire designed to assess the subjective bothersomeness and functional disruptiveness of nocturia. The Hsu 5 point Likert Bother Scale was scored from 0 (not at all) to 4 (extremely).

Change from baseline in visit-specific Hsu Bother is presented in this endpoint.

Level estimated for baseline value of Hsu Bother equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[194] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	23	22	13
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.896 (-1.161 to -0.630)	-0.940 (-1.294 to -0.586)	-0.712 (-1.083 to -0.340)	-0.606 (-1.079 to -0.132)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	27	68	
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.096 (-1.698 to -0.493)	-0.861 (-1.193 to -0.530)	-0.665 (-0.885 to -0.445)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1583 [195]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.551
upper limit	0.09

Notes:

[195] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1884 [196]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.275
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.685
upper limit	0.136

Notes:
[196] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8256 [197]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.463
upper limit	0.369

Notes:
[197] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8198 [198]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.059
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.455
upper limit	0.574

Notes:
[198] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1793 [199]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.431

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.061
upper limit	0.199

Notes:

[199] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3155 [200]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.196
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.581
upper limit	0.189

Notes:

[200] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Hsu 5-point Likert Bother Scale at Week 8

End point title	Change From Baseline in Hsu 5-point Likert Bother Scale at Week 8[201]

End point description:

The Hsu 5-point Likert Bother scale is a questionnaire designed to assess the subjective bothersomeness and functional disruptiveness of nocturia. The Hsu 5 point Likert Bother Scale was scored from 0 (not at all) to 4 (extremely).

Change from baseline in visit-specific Hsu Bother is presented in this endpoint.

Level estimated for baseline value of Hsu Bother equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[201] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	24	23	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.972 (-1.273 to -0.672)	-1.044 (-1.423 to -0.664)	-0.991 (-1.389 to -0.594)	-0.499 (-1.001 to 0.004)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	27	71	
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.012 (-1.691 to -0.333)	-0.881 (-1.240 to -0.522)	-0.731 (-0.968 to -0.495)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.183 [202]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.241
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.596
upper limit	0.114

Notes:

[202] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1618 [203]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.313
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.751
upper limit	0.126

Notes:

[203] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2519 [204]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.706
upper limit	0.186

Notes:

[204] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4044 [205]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.232
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.316
upper limit	0.781

Notes:

[205] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4348 [206]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.986
upper limit	0.426

Notes:

[206] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4786 [207]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.565
upper limit	0.266

Notes:

[207] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Hsu 5-point Likert Bother Scale at Week 12

End point title	Change From Baseline in Hsu 5-point Likert Bother Scale at Week 12[208]

End point description:

The Hsu 5-point Likert Bother scale is a questionnaire designed to assess the subjective bothersomeness and functional disruptiveness of nocturia. The Hsu 5 point Likert Bother Scale was scored from 0 (not at all) to 4 (extremely).

Change from baseline in visit-specific Hsu Bother is presented in this endpoint.

Level estimated for baseline value of Hsu Bother equal to 3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[208] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	22	21	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.992 (-1.306 to -0.679)	-1.249 (-1.663 to -0.834)	-0.700 (-1.132 to -0.267)	-0.880 (-1.416 to -0.343)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	28	67	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.974 (-1.676 to -0.272)	-0.921 (-1.303 to -0.540)	-0.769 (-1.027 to -0.511)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2412 [209]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.223
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.598
upper limit	0.151

Notes:

[209] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0501 [210]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.959
upper limit	0

Notes:

[210] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7788 [211]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.069
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.417
upper limit	0.556

Notes:

[211] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7111 [212]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.111
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.698
upper limit	0.477

Notes:

[212] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5816 [213]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.205
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.937
upper limit	0.527

Notes:

[213] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4981 [214]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.152
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.595
upper limit	0.29

Notes:

[214] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in ISI at Week 4

End point title	Change From Baseline in ISI at Week 4[215]

End point description:

The ISI is a 7-item questionnaire which comprises of four `sleep-related' items and three `wake-related' items. Each item is rated on a 0-4 scale and the total score ranges from 0 to 28 (higher score suggests more severe insomnia).

Change from baseline in visit-specific ISI is presented in this endpoint.

Level estimated for baseline value of ISI equal to 15 is presented in this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[215] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	24	22	13
Units: score on a scale				
least squares mean (confidence interval 95%)	-6.589 (-8.046 to -5.133)	-6.652 (-8.689 to -4.616)	-5.630 (-7.772 to -3.487)	-5.428 (-8.200 to -2.656)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	27	68	
Units: score on a scale				
least squares mean (confidence interval 95%)	-4.510 (-7.996 to -1.023)	-6.372 (-8.291 to -4.452)	-5.277 (-6.493 to -4.061)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1733 [216]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.313
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.207
upper limit	0.582

Notes:

[216] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo

Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2538 [217]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.375
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.745
upper limit	0.994

Notes:

[217] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7782 [218]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.353
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.818
upper limit	2.113

Notes:

[218] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9218 [219]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.151
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.182
upper limit	2.88

Notes:

[219] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6823 [220]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.767
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.923
upper limit	4.457

Notes:

[220] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3436 [221]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.095
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.369
upper limit	1.179

Notes:

[221] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in ISI at Week 8

End point title	Change From Baseline in ISI at Week 8[222]

End point description:

The ISI is a 7-item questionnaire which comprises of four `sleep-related' items and three `wake-related' items. Each item is rated on a 0-4 scale and the total score ranges from 0 to 28 (higher score suggests more severe insomnia).

Change from baseline in visit-specific ISI is presented in this endpoint.

Level estimated for baseline value of ISI equal to 15 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[222] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	24	23	14
Units: units on a scale				
least squares mean (confidence interval 95%)	-7.643 (-9.140 to -6.147)	-8.091 (-10.116 to -6.067)	-6.693 (-8.799 to -4.588)	-6.959 (-9.668 to -4.250)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	28	71	
Units: units on a scale				
least squares mean (confidence interval 95%)	-5.707 (-9.283 to -2.131)	-7.167 (-9.055 to -5.280)	-6.408 (-7.603 to -5.213)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2042 [223]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.235
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.146
upper limit	0.676

Notes:
[223] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1591 [224]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.683
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.031
upper limit	0.665

Notes:
[224] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8168 [225]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.285
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.708
upper limit	2.138

Notes:
[225] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7148 [226]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.551

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.517
upper limit	2.416

Notes:

[226] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7141 [227]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.701
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.066
upper limit	4.468

Notes:

[227] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5041 [228]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-0.759
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.995
upper limit	1.477

Notes:

[228] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in ISI at Week 12

End point title	Change From Baseline in ISI at Week 12[229]

End point description:

The ISI is a 7-item questionnaire which comprises of four `sleep-related' items and three `wake-related' items. Each item is rated on a 0-4 scale and the total score ranges from 0 to 28 (higher score suggests more severe insomnia).

Change from baseline in visit-specific ISI is presented in this endpoint.

Level estimated for baseline value of ISI equal to 15 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[229] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	22	21	14
Units: score on a scale				
least squares mean (confidence interval 95%)	-7.807 (-9.427 to -6.188)	-9.329 (-11.619 to -7.040)	-6.355 (-8.733 to -3.977)	-6.193 (-9.195 to -3.191)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	27	67	
Units: score on a scale				
least squares mean (confidence interval 95%)	-5.002 (-8.865 to -1.138)	-7.908 (-10.016 to -5.800)	-6.678 (-8.018 to -5.338)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2896 [230]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.129

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.226
upper limit	0.967

Notes:

[230] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0498 [231]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-2.652
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.301
upper limit	-0.003

Notes:

[231] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8159 [232]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.323
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.409
upper limit	3.055

Notes:

[232] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7719 [233]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	0.485
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.809
upper limit	3.779

Notes:

[233] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4193 [234]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	1.676
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.407
upper limit	5.76

Notes:

[234] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3333 [235]
Method	MMRM
Parameter estimate	Least Square Mean Difference
Point estimate	-1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.73
upper limit	1.27

Notes:

[235] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Duration of First Undisturbed Sleep Period (FUSP) at Week 1

End point title	Change From Baseline in Mean Duration of First Undisturbed Sleep Period (FUSP) at Week 1[236]

End point description:

The FUSP is defined as the time in minutes from the time of going to bed to the time of first nocturnal void, or time of awakening if no void occured.
The duration of FUSP at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in FUSP are estimated using a baseline value of 180 (min).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[236] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	24	24	14
Units: minutes				
least squares mean (confidence interval 95%)	122.9 (86.2 to 159.7)	187.0 (132.3 to 241.7)	106.0 (49.6 to 162.4)	91.7 (18.7 to 164.8)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	33	80	
Units: minutes				
least squares mean (confidence interval 95%)	82.9 (2.5 to 163.4)	51.3 (3.9 to 98.7)	81.1 (50.8 to 111.4)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0853 [237]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	41.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	89.6

Notes:

[237] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [238]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	105.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.4
upper limit	168.4

Notes:

[238] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4418 [239]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	24.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.8
upper limit	88.6

Notes:

[239] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7902 [240]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.2
upper limit	89.6

Notes:

[240] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9664 [241]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-84.2
upper limit	87.9

Notes:

[241] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2977 [242]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-29.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-85.9
upper limit	26.4

Notes:

[242] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Duration of FUSP at Week 4

End point title	Change From Baseline in Mean Duration of FUSP at Week 4[243]

End point description:

The FUSP is defined as the time in minutes from the time of going to bed to the time of first nocturnal void, or time of awakening if no void occurred.

The duration of FUSP at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in FUSP are estimated using a baseline value of 180 (min).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[243] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	22	21	12
Units: minutes				
arithmetic mean (confidence interval 95%)	164.5 (127.9 to 201.0)	211.0 (156.3 to 265.7)	132.3 (75.2 to 189.4)	89.5 (15.1 to 163.9)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	31	76	
Units: minutes				
arithmetic mean (confidence interval 95%)	122.0 (46.8 to 197.3)	95.5 (48.6 to 142.5)	150.2 (120.4 to 180.0)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5523 [244]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33
upper limit	61.5

Notes:

[244] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0556 [245]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	60.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	123

Notes:

[245] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5837 [246]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-17.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-82
upper limit	46.3

Notes:

[246] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1363 [247]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-60.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-140.7
upper limit	19.3

Notes:

[247] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4938 [248]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-28.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-109.1
upper limit	52.8

Notes:

[248] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0535 [249]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-54.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-110.2
upper limit	0.8

Notes:

[249] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Duration of FUSP at Week 8

End point title	Change From Baseline in Mean Duration of FUSP at Week 8[250]

End point description:

The FUSP is defined as the time in minutes from the time of going to bed to the time of first nocturnal void, or time of awakening if no void occurred.

The duration of FUSP at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in FUSP are estimated using a baseline value of 180 (min).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 8

Notes:

[250] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	23	21	14
Units: minutes				
arithmetic mean (confidence interval 95%)	160.4 (112.4 to 208.3)	225.4 (157.9 to 293.0)	190.2 (118.9 to 261.6)	136.8 (48.3 to 225.4)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	30	70	
Units: minutes				
arithmetic mean (confidence interval 95%)	163.2 (68.7 to 257.8)	164.3 (104.9 to 223.7)	161.0 (122.6 to 199.5)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9829 [251]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.2
upper limit	60.9

Notes:

[251] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1038 [252]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	64.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	142.1

Notes:

[252] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4764 [253]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	29.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.4
upper limit	109.8

Notes:

[253] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6204 [254]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-120.5
upper limit	72

Notes:

[254] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.966 [255]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-100.1
upper limit	104.6

Notes:

[255] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9275 [256]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.4
upper limit	73.9

Notes:

[256] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean Duration of FUSP at Week 12

End point title	Change From Baseline in Mean Duration of FUSP at Week

End point description:

The FUSP is defined as the time in minutes from the time of going to bed to the time of first nocturnal void, or time of awakening if no void occurred.

The duration of FUSP at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in FUSP are estimated using a baseline value of 180 (min).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[257] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	19	19	14
Units: minutes				
arithmetic mean (confidence interval 95%)	178.5 (132.5 to 224.5)	160.0 (93.3 to 226.6)	180.7 (112.2 to 249.2)	111.5 (29.7 to 193.2)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	29	69	
Units: minutes				
arithmetic mean (confidence interval 95%)	141.1 (51.3 to 230.9)	166.2 (110.5 to 221.8)	162.8 (126.9 to 198.7)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5964 [258]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.7
upper limit	74.2

Notes:

[258] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 350 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9418 [259]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.5
upper limit	72.9

Notes:

[259] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 250 µg (Randomised Treatment Period)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6452 [260]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.8
upper limit	94.7

Notes:

[260] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 150 µg (Randomised Treatment Period)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2565 [261]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-51.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-140.2
upper limit	37.6

Notes:

[261] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 100 µg (Randomised Treatment Period)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6605 [262]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-21.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-118.6
upper limit	75.4

Notes:

[262] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	Placebo (Randomised Treatment Period) v FE 201836 50 µg (Randomised Treatment Period)
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9191 [263]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.6
upper limit	69.4

Notes:

[263] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Aggregated Mean Duration of FUSP During 12 Weeks of Treatment

End point title	Change From Baseline in Aggregated Mean Duration of FUSP During 12 Weeks of Treatment[264]

End point description:

The FUSP is defined as the time in minutes from the time of going to bed to the time of first nocturnal void, or time of awakening if no void occurred.

The visit-specific means were aggregated into a mean of current and preceding visits.

Level estimated for baseline value of mean duration of FUSP (minutes) equal to 180 is presented in this endpoint.

The 95% credibility interval (2.5 and 97.5 percentiles of the posterior distribution) instead of confidence interval is presented for this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, During 12 Weeks of Treatment

Notes:

[264] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	27	24	14
Units: minutes				
arithmetic mean (confidence interval 95%)	154.98 (130.41 to 189.10)	150.23 (130.20 to 181.15)	145.95 (128.21 to 170.90)	140.74 (120.51 to 160.16)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	34	87	
Units: minutes				
arithmetic mean (confidence interval 95%)	139.19 (117.86 to 157.42)	138.13 (115.62 to 157.24)	137.45 (114.12 to 157.30)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	17.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.19
upper limit	62.09

Statistical analysis title	FE 201836 350 ug, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	12.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	55.89

Statistical analysis title	FE 201836 250 ug, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	47.28

Statistical analysis title	FE 201836 150 ug, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	3.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	28.07

Statistical analysis title	FE 201836 100 ug, Placebo
Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	17.9

Statistical analysis title	FE 201836 50 ug, Placebo

Statistical analysis description:	
Based on a Bayesian analysis of a sigmoidal dose-response relationship.	
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean Difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	7.55

Secondary: Change From Baseline in Nocturnal Diuresis Rate Profiles at Week 1

End point title	Change From Baseline in Nocturnal Diuresis Rate Profiles at Week 1[265]

End point description:

The nocturnal diuresis rate (mL/min) is calculated as the mean of the nocturnal diuresis for each of the three nights, with the single-night nocturnal diuresis calculated as the ratio of NUV to total time in bed.

Change from baseline in visit-specific mean nocturnal diuresis (mL/min) is presented.

Level estimated for baseline value of mean nocturnal diuresis (mL/min) equal to 1.3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[265] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	24	24	14
Units: mL/min				
arithmetic mean (confidence interval 95%)	-0.575 (-0.687 to -0.463)	-0.635 (-0.801 to -0.468)	-0.610 (-0.779 to -0.440)	-0.459 (-0.678 to -0.239)

End point values	FE 201836 100 µg (Randomised	FE 201836 50 µg (Randomised	Placebo (Randomised Treatment	

	Treatment Period)	Treatment Period)	Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	32	78	
Units: mL/min				
arithmetic mean (confidence interval 95%)	-0.523 (-0.766 to -0.280)	-0.328 (-0.474 to -0.182)	-0.402 (-0.494 to -0.310)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0196 [266]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.173
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.318
upper limit	-0.028

Notes:

[266] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0167 [267]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.233
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.423
upper limit	-0.043

Notes:

[267] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0352 [268]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.208
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.401
upper limit	-0.015

Notes:

[268] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6402 [269]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.295
upper limit	0.182

Notes:

[269] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3602 [270]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.121
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.381
upper limit	0.139

Notes:

[270] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4018 [271]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.099
upper limit	0.247

Notes:

[271] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Nocturnal Diuresis Rate Profiles at Week 12

End point title	Change From Baseline in Nocturnal Diuresis Rate Profiles at Week 12[272]

End point description:

The nocturnal diuresis rate (mL/min) is calculated as the mean of the nocturnal diuresis for each of the three nights, with the single-night nocturnal diuresis calculated as the ratio of NUV to total time in bed.

Change from baseline in visit-specific mean nocturnal diuresis (mL/min) is presented.

Level estimated for baseline value of mean nocturnal diuresis (mL/min) equal to 1.3 is presented in this endpoint.

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[272] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	18	18	14
Units: mL/min				
arithmetic mean (confidence interval 95%)	-0.648 (-0.789 to -0.508)	-0.606 (-0.805 to -0.408)	-0.735 (-0.937 to -0.533)	-0.458 (-0.693 to -0.223)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	29	68	
Units: mL/min				
arithmetic mean (confidence interval 95%)	-0.685 (-0.945 to -0.425)	-0.651 (-0.812 to -0.490)	-0.515 (-0.619 to -0.412)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1354 [273]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.133
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.308
upper limit	0.042

Notes:

[273] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4238 [274]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.091
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.315
upper limit	0.133

Notes:

[274] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo

Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0574 [275]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.446
upper limit	0.007

Notes:

[275] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6579 [276]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	0.058
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.199
upper limit	0.315

Notes:

[276] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2337 [277]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.11

Notes:

[277] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1639 [278]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-0.136
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.328
upper limit	0.056

Notes:

[278] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Mean NUV in Week 1

End point title	Change From Baseline in Mean NUV in Week 1[279]

End point description:

The NUV is defined as the total urine volume from 5 minutes after bedtime with the intention to sleep including the first void within 30 minutes of rising in the morning.

The NUV at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NUV are estimated using a baseline value of 750 (mL).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 1

Notes:

[279] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	24	24	14
Units: mL				
arithmetic mean (confidence interval 95%)	-328.8 (-395.3 to -262.3)	-371.8 (-470.4 to -273.3)	-352.4 (-452.8 to -252.1)	-265.5 (-395.5 to -135.6)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	32	78	
Units: mL				
arithmetic mean (confidence interval 95%)	-312.6 (-455.9 to -169.3)	-218.2 (-304.9 to -131.6)	-241.6 (-296.3 to -186.9)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-87.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-173.2
upper limit	-1.2

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0237
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-130.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-242.9
upper limit	-17.6

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0569
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-110.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-224.9
upper limit	3.3

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7383
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-23.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-164.8
upper limit	117

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3626
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-224.3
upper limit	82.3

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6524
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	23.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.9
upper limit	125.7

Secondary: Change From Baseline in Mean NUV at Week 12

End point title	Change From Baseline in Mean NUV at Week 12[280]

End point description:

The NUV is defined as the total urine volume from 5 minutes after bedtime with the intention to sleep including the first void within 30 minutes of rising in the morning.

The NUV at each visit was calculated as the average over the 3 consecutive 24-hour periods just prior to the respective visit. Adjusted visit-specific mean changes from baseline in NUV are estimated using a baseline value of 750 (mL).

The analysis population included ITT-RT which comprised of all the subjects randomised at Visit 4.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[280] - 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: Treatment comparison refers to the pair-wise comparison between active treatment (the different doses of FE 201836) and placebo. Desmopressin was included as a benchmark treatment only. None of the secondary analyses included data from subjects treated with desmopressin.

End point values	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	18	18	14
Units: mL				
arithmetic mean (confidence interval 95%)	-367.3 (-447.1 to -287.5)	-392.4 (-505.2 to -279.5)	-411.3 (-526.0 to -296.7)	-284.2 (-418.4 to -149.9)

End point values	FE 201836 100 µg (Randomised Treatment Period)	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	29	68	
Units: mL				
arithmetic mean (confidence interval 95%)	-393.5 (-541.9 to -245.1)	-403.2 (-495.5 to -310.9)	-317.8 (-377.1 to -258.5)	

Statistical analyses

Statistical analysis title	FE 201836 500 ug, Placebo
Comparison groups	FE 201836 500 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3273 [281]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-49.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-148.9
upper limit	49.9

Notes:

[281] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 350 ug, Placebo
Comparison groups	FE 201836 350 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25 [282]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-74.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-202
upper limit	52.9

Notes:

[282] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 250 ug, Placebo
Comparison groups	FE 201836 250 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1537 [283]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-93.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-222.3
upper limit	35.2

Notes:

[283] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 150 ug, Placebo
Comparison groups	FE 201836 150 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6515 [284]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	33.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-113.1
upper limit	180.3

Notes:

[284] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 100 ug, Placebo
Comparison groups	FE 201836 100 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3506 [285]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-75.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-235.3
upper limit	83.9

Notes:

[285] - Threshold for significance at 0.05 level.

Statistical analysis title	FE 201836 50 ug, Placebo
Comparison groups	FE 201836 50 µg (Randomised Treatment Period) v Placebo (Randomised Treatment Period)
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1255 [286]
Method	MMRM
Parameter estimate	Mean Difference
Point estimate	-85.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-194.8
upper limit	24.1

Notes:

[286] - Threshold for significance at 0.05 level.

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) occurring in time interval from V2 (active run-in) to V4 (randomisation), including AEs with missing start date were considered 'enrichment-treatment emergent'. AEs occurring from V4 to end-of-trial were considered 'treatment-emergent'

Adverse event reporting additional description:

The Safety Analysis Set for enrichment period comprised subjects who received investigational medicinal product (IMP) at V2 and did not return all IMP unused at/before V4. Safety Analysis Set for randomised treatment period comprised subjects who received IMP at V4 and did not return all IMP unused, and who had at least 1 safety assessment after V4

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	FE 201836 500 µg (Enrichment Period)

Reporting group description:

FE 201836 500 µg oral solution and placebo ODT

Reporting group title	FE 201836 500 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 500 µg oral solution and placebo ODT

Reporting group title	FE 201836 350 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 350 µg oral solution and placebo ODT

Reporting group title	FE 201836 250 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 250 µg oral solution and placebo ODT

Reporting group title	FE 201836 150 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 150 µg oral solution and placebo ODT

Reporting group title	FE 201836 100 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 100 µg oral solution and placebo ODT

Reporting group title	FE 201836 50 µg (Randomised Treatment Period)

Reporting group description:

FE 201836 50 µg oral solution and placebo ODT

Reporting group title	Placebo (Randomised Treatment Period)

Reporting group description:

Placebo oral solution and placebo ODT

Reporting group title	Desmopressin 25 µg (Randomised Treatment Period)

Reporting group description:

Desmopressin 25 µg ODT and placebo oral solution

Reporting group title	Desmopressin 50 µg (Randomised Treatment Period)

Reporting group description:

Desmopressin 50 µg ODT and placebo oral solution

Serious adverse events	FE 201836 500 µg (Enrichment Period)	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 531 (0.38%)	1 / 60 (1.67%)	2 / 27 (7.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Serum sickness-like reaction			
subjects affected / exposed	0 / 531 (0.00%)	1 / 60 (1.67%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 531 (0.38%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)	FE 201836 100 µg (Randomised Treatment Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 14 (0.00%)	1 / 13 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 24 (4.17%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 24 (4.17%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			

subjects affected / exposed	1 / 24 (4.17%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Serum sickness-like reaction			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	Desmopressin 25 µg (Randomised Treatment Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	2 / 87 (2.30%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Facial bones fracture			

subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Serum sickness-like reaction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			

subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Desmopressin 50 µg (Randomised Treatment Period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Serum sickness-like reaction			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	0 / 17 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	FE 201836 500 µg (Enrichment Period)	FE 201836 500 µg (Randomised Treatment Period)	FE 201836 350 µg (Randomised Treatment Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 531 (0.00%)	16 / 60 (26.67%)	3 / 27 (11.11%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 531 (0.00%)	1 / 60 (1.67%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight increased			
subjects affected / exposed	0 / 531 (0.00%)	3 / 60 (5.00%)	0 / 27 (0.00%)
occurrences (all)	0	3	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 531 (0.00%)	2 / 60 (3.33%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 531 (0.00%)	2 / 60 (3.33%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 531 (0.00%)	3 / 60 (5.00%)	0 / 27 (0.00%)
occurrences (all)	0	4	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 531 (0.00%)	1 / 60 (1.67%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 531 (0.00%)	3 / 60 (5.00%)	1 / 27 (3.70%)
occurrences (all)	0	3	1
Diarrhoea			
subjects affected / exposed	0 / 531 (0.00%)	2 / 60 (3.33%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 531 (0.00%)	2 / 60 (3.33%)	0 / 27 (0.00%)
occurrences (all)	0	3	0
Joint swelling			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 531 (0.00%)	3 / 60 (5.00%)	0 / 27 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 531 (0.00%)	3 / 60 (5.00%)	2 / 27 (7.41%)
occurrences (all)	0	5	2
Hypoglycaemia			
subjects affected / exposed	0 / 531 (0.00%)	0 / 60 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	FE 201836 250 µg (Randomised Treatment Period)	FE 201836 150 µg (Randomised Treatment Period)	FE 201836 100 µg (Randomised Treatment Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 24 (12.50%)	8 / 14 (57.14%)	5 / 13 (38.46%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	2 / 14 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	2 / 14 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)	2 / 14 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Blood alkaline phosphatase			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 24 (4.17%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hand fracture			

subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 24 (8.33%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 24 (0.00%)	2 / 14 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Renal impairment			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 24 (4.17%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 14 (7.14%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 14 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	FE 201836 50 µg (Randomised Treatment Period)	Placebo (Randomised Treatment Period)	Desmopressin 25 µg (Randomised Treatment Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 34 (20.59%)	16 / 87 (18.39%)	8 / 26 (30.77%)
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 34 (2.94%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 34 (0.00%)	2 / 87 (2.30%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Investigations			
Weight increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Blood sodium decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Alanine aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 34 (2.94%)	3 / 87 (3.45%)	0 / 26 (0.00%)
occurrences (all)	1	4	0
Hand fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 34 (2.94%)	2 / 87 (2.30%)	1 / 26 (3.85%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 34 (2.94%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 34 (2.94%)	0 / 87 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 34 (2.94%)	3 / 87 (3.45%)	0 / 26 (0.00%)
occurrences (all)	1	4	0
Diarrhoea			

subjects affected / exposed	1 / 34 (2.94%)	1 / 87 (1.15%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Renal impairment			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 87 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 87 (1.15%)	0 / 26 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Desmopressin 50 µg (Randomised Treatment Period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 17 (52.94%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Investigations			
Weight increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood sodium decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	6		
Hand fracture			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	3		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 17 (0.00%)		
occurrences (all)	0		
Myalgia			

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Cellulitis subjects affected / exposed occurrences (all)	 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0		
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2017	The reason for this protocol amendment was to implement changes to the clinical trial protocol in agreement with Competent Authorities and Independent Ethics Committees in countries where the trial was conducted, following review of Clinical Trial Protocol version 2.0, dated 04 January 2017.
05 July 2018	The reason for this protocol amendment was to update according to recent guidelines and research within lower urinary tract symptoms (LUTS) and to enhance subject recruitment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported