



Clinical trial results:

A phase II, randomised, double-blind, placebo-controlled, parallel-group, multi-centre study investigating efficacy and safety of Sepranolone (UC1010) in patients with PMDD

Summary

EudraCT number	2017-000822-37
Trial protocol	GB DE SE PL
Global end of trial date	25 February 2020

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021
Summary attachment (see zip file)	UM203 Asarina CSR Synopsis (Asarina_UM203_CSR Synopsis_final v1.0_23OCT2020.pdf)

Trial information

Trial identification

Sponsor protocol code	UM203
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Asarina Pharma
Sponsor organisation address	c/o COBIS, Ole Maaloos Vej 3, Copenhagen, Denmark, 2200
Public contact	Karin Ekberg, Asarina Pharma , +45 707029 80 , karin.ekberg@asarinapharma.com
Scientific contact	Karin Ekberg, Asarina Pharma , +45 707029 80 , karin.ekberg@asarinapharma.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	17 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2020
Global end of trial reached?	Yes
Global end of trial date	25 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the effect of two doses of UC1010 on premenstrual symptoms in women with PMDD in comparison to placebo.

The effect of UC1010 given repeatedly to women with PMDD as subcutaneous injections during the luteal phase of three consecutive menstrual cycles will be compared with a corresponding placebo administration. Effect will be assessed by comparison of symptoms recorded daily by the patients using a validated rating scale also used for the diagnosis of PMDD.

Protection of trial subjects:

The clinical safety of the patient was followed throughout their participation in the study with physical examinations (including vital signs and inspection of injection sites), safety blood sampling and AE and concomitant medication reporting. The reporting of AEs started when the first dose of IMP was taken and continued until visit 9, i.e. the close-out visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Sweden: 46
Country: Number of subjects enrolled	United Kingdom: 54
Country: Number of subjects enrolled	Germany: 78
Worldwide total number of subjects	206
EEA total number of subjects	206

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)	206
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment started on 20 April 2018 and was completed in November 2019. Subjects from Germany, Sweden, Poland, and UK were recruited into the study

Pre-assignment

Screening details:

475 patients enrolled, 206 randomised. 4 randomised patients never started treatment. Patients underwent a qualification period for PMDD diagnosis of at least 2 menstrual cycles.

Screening criteria included: previous participation, height, weight, menstrual cycle details/symptoms, other medications/condition

Pre-assignment period milestones

Number of subjects started	475 ^[1]
Number of subjects completed	202

Pre-assignment subject non-completion reasons

Reason: Number of subjects	screen failure: 269
Reason: Number of subjects	subjects never started treatment: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects enrolled is counted as the number randomised and assigned to a treatment arm. A greater number signed the ICF and underwent a 2 month qualification period, but did not meet the criteria for PMDD diagnosis and therefore did not qualify for the study.

Period 1

Period 1 title	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	Sepranolone 10 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Sepranolone
Investigational medicinal product code	
Other name	UC1010
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

10 mg per injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

Arm title	Sepranolone 16 mg
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	Sepranolone
Investigational medicinal product code	
Other name	UC1010
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

16 mg per injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo injection once every second day during the luteal phase of 3 consecutive menstrual cycles to women with a verified diagnosis of PMDD. Treatment will start 14 days prior to the next estimated menstruation start and continue until menstruation starts, but with a maximum of 7 doses per cycle. The treatment period is followed by one menstrual cycle of non-treatment as a follow-up cycle.

Number of subjects in period 1^[2]	Sepranolone 10 mg	Sepranolone 16 mg	Placebo
Started	64	68	70
Completed	53	54	58
Not completed	11	14	12
Consent withdrawn by subject	3	7	2
other reasons	-	2	-
Adverse event, non-fatal	5	3	4
Pregnancy	-	-	1
Lost to follow-up	3	2	2
other reason	-	-	3

Notes:

[2] - 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: 206 subjects enrolled in the study and were randomised into a treatment arm, but only 202 started treatment and are included in the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	Sepranolone 10 mg
Reporting group description: -	
Reporting group title	Sepranolone 16 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Sepranolone 10 mg	Sepranolone 16 mg	Placebo
Number of subjects	64	68	70
Age categorical			
All subjects were aged 18 to 45 years at first visit			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18 to 45 years	64	68	70
Age continuous			
Units: years			
arithmetic mean	32.72	33.35	34.14
full range (min-max)	23 to 44.6	20.3 to 44.7	22.4 to 44.6
Gender categorical			
All patients were female			
Units: Subjects			
Female	64	68	70
Male	0	0	0
Race			
Units: Subjects			
White	61	64	67
Other	3	3	2
Black or African American	0	1	1
Smoker Status			
Units: Subjects			
Non-smoker	34	43	40
Ex-smoker	11	13	17
Smoker	19	12	13
Previous PMDD treatment			
Units: Subjects			
Yes	17	20	17

No	47	48	53
History of psychiatric disorders Units: Subjects			
Yes	11	18	11
No	53	50	59
History of PMDD diagnosis Units: Subjects			
Yes	11	10	16
No	53	58	54
BMI Units: mg/kg2			
arithmetic mean	24.13	24.22	24.79
full range (min-max)	18.5 to 34.7	16.6 to 34.6	18.4 to 34.4
PMDD History Units: years			
arithmetic mean	10.08	9.08	9.53
full range (min-max)	2 to 27	2 to 24	1 to 30
Baseline Total Symptoms			
LmaxSum21			
Units: points			
arithmetic mean	82.25	87.3	85.46
full range (min-max)	56.5 to 118.7	52.1 to 122.4	53.7 to 123.3
Baseline symptoms in follicular phase			
FminSum21			
Units: points			
arithmetic mean	23.96	23.53	23.39
full range (min-max)	21 to 33.6	21 to 30.9	21 to 33.5

Reporting group values	Total		
Number of subjects	202		
Age categorical			
All subjects were aged 18 to 45 years at first visit			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
18 to 45 years	202		
Age continuous Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
All patients were female			
Units: Subjects			

Female	202		
Male	0		
Race			
Units: Subjects			
White	192		
Other	8		
Black or African American	2		
Smoker Status			
Units: Subjects			
Non-smoker	117		
Ex-smoker	41		
Smoker	44		
Previous PMDD treatment			
Units: Subjects			
Yes	54		
No	148		
History of psychiatric disorders			
Units: Subjects			
Yes	40		
No	162		
History of PMDD diagnosis			
Units: Subjects			
Yes	37		
No	165		
BMI			
Units: mg/kg ²			
arithmetic mean			
full range (min-max)	-		
PMDD History			
Units: years			
arithmetic mean			
full range (min-max)	-		
Baseline Total Symptoms			
LmaxSum21			
Units: points			
arithmetic mean			
full range (min-max)	-		
Baseline symptoms in follicular phase			
FminSum21			
Units: points			
arithmetic mean			
full range (min-max)	-		

Subject analysis sets

Subject analysis set title	Safety Analysis Set - Sepranolone 10mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 10mg	

Subject analysis set title	Safety Analysis Set - Sepranolone 16mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 16mg	
Subject analysis set title	Safety Analysis Set - placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set includes all subjects who obtained at least one dose of the placebo	
Subject analysis set title	Intent to Treat Sepranolone 10mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg	
Subject analysis set title	Intent to Treat Sepranolone 16mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 16mg	
Subject analysis set title	Intent to Treat Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Placebo	
Subject analysis set title	Intent to Treat Active
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg or 16mg	

Reporting group values	Safety Analysis Set - Sepranolone 10mg	Safety Analysis Set - Sepranolone 16mg	Safety Analysis Set - placebo
Number of subjects	64	68	70
Age categorical			
All subjects were aged 18 to 45 years at first visit			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18 to 45 years	64	68	70
Age continuous			
Units: years			
arithmetic mean	34.14	32.72	33.35
full range (min-max)	22.4 to 44.6	23 to 44.6	20.3 to 44.7

Gender categorical			
All patients were female			
Units: Subjects			
Female	64	68	70
Male	0	0	0
Race			
Units: Subjects			
White	61	64	67
Other	3	3	2
Black or African American	0	1	1
Smoker Status			
Units: Subjects			
Non-smoker	34	43	40
Ex-smoker	19	12	13
Smoker	11	13	17
Previous PMDD treatment			
Units: Subjects			
Yes	17	17	20
No	47	48	53
History of psychiatric disorders			
Units: Subjects			
Yes	11	18	11
No	53	50	59
History of PMDD diagnosis			
Units: Subjects			
Yes	11	10	16
No	53	58	54
BMI			
Units: mg/kg2			
arithmetic mean	24.13	24.22	24.79
full range (min-max)	18.5 to 34.7	16.6 to 34.6	18.4 to 34.4
PMDD History			
Units: years			
arithmetic mean	10.08	9.08	9.53
full range (min-max)	2 to 27	2 to 24	1 to 30
Baseline Total Symptoms			
LmaxSum21			
Units: points			
arithmetic mean	82.25	87.3	85.46
full range (min-max)	56.5 to 118.7	52.1 to 122.4	53.7 to 123.3
Baseline symptoms in follicular phase			
FminSum21			
Units: points			
arithmetic mean	23.96	23.53	23.39
full range (min-max)	21 to 33.6	21 to 30.9	21 to 33.5
Reporting group values	Intent to Treat Sepranolone 10mg	Intent to Treat Sepranolone 16mg	Intent to Treat Placebo
Number of subjects	63	62	67
Age categorical			
All subjects were aged 18 to 45 years at first visit			
Units: Subjects			

In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18 to 45 years	63	62	67
Age continuous			
Units: years			
arithmetic mean	32.7	33.2	34.35
full range (min-max)	23 to 44.6	20.3 to 43	22.4 to 44.6
Gender categorical			
All patients were female			
Units: Subjects			
Female	63	62	67
Male	0	0	0
Race			
Units: Subjects			
White	60	58	64
Other	3	3	2
Black or African American	0	1	1
Smoker Status			
Units: Subjects			
Non-smoker	34	40	38
Ex-smoker	11	11	16
Smoker	18	11	13
Previous PMDD treatment			
Units: Subjects			
Yes	17	19	16
No	46	43	51
History of psychiatric disorders			
Units: Subjects			
Yes	11	18	11
No	52	44	56
History of PMDD diagnosis			
Units: Subjects			
Yes	11	9	16
No	52	53	51
BMI			
Units: mg/kg2			
arithmetic mean	24.19	24.24	24.82
full range (min-max)	18.5 to 34.7	16.6 to 34.6	18.4 to 34.4
PMDD History			
Units: years			
arithmetic mean	10	8.8	9.66
full range (min-max)	2 to 27	2 to 22	1 to 30
Baseline Total Symptoms			

LmaxSum21			
Units: points			
arithmetic mean	82.35	87.13	85.05
full range (min-max)	56.5 to 118.7	52.1 to 122.4	53.7 to 123.3
Baseline symptoms in follicular phase			
FminSum21			
Units: points			
arithmetic mean	24.01	23.42	23.36
full range (min-max)	21 to 33.6	21 to 30.6	21 to 33.5

Reporting group values	Intent to Treat Active		
Number of subjects	125		
Age categorical			
All subjects were aged 18 to 45 years at first visit			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
18 to 45 years	125		
Age continuous			
Units: years			
arithmetic mean	32.94		
full range (min-max)	20.3 to 44.6		
Gender categorical			
All patients were female			
Units: Subjects			
Female	125		
Male	0		
Race			
Units: Subjects			
White	118		
Other	6		
Black or African American	1		
Smoker Status			
Units: Subjects			
Non-smoker	74		
Ex-smoker	22		
Smoker	29		
Previous PMDD treatment			
Units: Subjects			
Yes	36		
No	89		
History of psychiatric disorders			
Units: Subjects			

Yes	29		
No	96		
History of PMDD diagnosis			
Units: Subjects			
Yes	20		
No	105		
BMI			
Units: mg/kg2			
arithmetic mean	24.21		
full range (min-max)	16.6 to 34.7		
PMDD History			
Units: years			
arithmetic mean	9.41		
full range (min-max)	2 to 27		
Baseline Total Symptoms			
LmaxSum21			
Units: points			
arithmetic mean	84.72		
full range (min-max)	52.1 to 122.4		
Baseline symptoms in follicular phase			
FminSum21			
Units: points			
arithmetic mean	23.72		
full range (min-max)	21 to 33.6		

End points

End points reporting groups

Reporting group title	Sepranolone 10 mg
Reporting group description: -	
Reporting group title	Sepranolone 16 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Safety Analysis Set - Sepranolone 10mg
Subject analysis set type	Safety analysis
Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 10mg	
Subject analysis set title	Safety Analysis Set - Sepranolone 16mg
Subject analysis set type	Safety analysis
Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the investigational drug at a dose of 16mg	
Subject analysis set title	Safety Analysis Set - placebo
Subject analysis set type	Safety analysis
Subject analysis set description: The safety analysis set includes all subjects who obtained at least one dose of the placebo	
Subject analysis set title	Intent to Treat Sepranolone 10mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg	
Subject analysis set title	Intent to Treat Sepranolone 16mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 16mg	
Subject analysis set title	Intent to Treat Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Placebo	
Subject analysis set title	Intent to Treat Active
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects with at least one confirmed ovulatory treatment cycle and had evaluable DSRP data in that cycle who received Sepranolone 10mg or 16mg	

Primary: Change in LmaxSum21 score before and during treatment

End point title	Change in LmaxSum21 score before and during treatment
End point description:	
End point type	Primary
End point timeframe: Within-subject differences were calculated by taking the average LmaxSum21 from the 2nd and the 3rd treatment cycles and subtracting the average LmaxSum21 from the two menstrual cycles D1 and D2	

End point values	Intent to Treat Sepranolone 10mg	Intent to Treat Sepranolone 16mg	Intent to Treat Placebo	Intent to Treat Active
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	63	62	67	125
Units: LmaxSum21 (points)				
arithmetic mean (full range (min-max))	-30.53 (-90.1 to 32.2)	-30.02 (-77.7 to 9)	-27.88 (-90.7 to 11)	-30.28 (-90.1 to 32.2)

Statistical analyses

Statistical analysis title	Primary confirmatory efficacy analysis
<p>Statistical analysis description:</p> <p>The primary confirmatory efficacy analysis proceeded in a hierarchical rejecting way. The null hypotheses were each tested at a two-sided type I error of $\alpha = 0.05$, but subsequent hypotheses were only tested if the previous null hypothesis had been rejected. Using this closed testing procedure, no alpha adjustment had to be applied to control the family-wise error rate of 5%.</p>	
Comparison groups	Intent to Treat Placebo v Intent to Treat Active
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3465
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of IMP to last visit (follow-up).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Sepranolone 10 mg
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Reporting group description: -

Reporting group title	Sepranolone 16 mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Sepranolone 10 mg	Sepranolone 16 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)	1 / 68 (1.47%)	1 / 70 (1.43%)
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)			
Breast cancer			
subjects affected / exposed	0 / 64 (0.00%)	1 / 68 (1.47%)	0 / 70 (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
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 64 (0.00%)	0 / 68 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Sepranolone 10 mg	Sepranolone 16 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 64 (26.56%)	33 / 68 (48.53%)	18 / 70 (25.71%)

Nervous system disorders Headache subjects affected / exposed occurrences (all)	6 / 64 (9.38%) 9	4 / 68 (5.88%) 6	8 / 70 (11.43%) 11
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all)	3 / 64 (4.69%) 15 2 / 64 (3.13%) 3	5 / 68 (7.35%) 16 8 / 68 (11.76%) 59	1 / 70 (1.43%) 3 3 / 70 (4.29%) 27
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0 0 / 64 (0.00%) 0	1 / 68 (1.47%) 1 4 / 68 (5.88%) 4	6 / 70 (8.57%) 7 0 / 70 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 64 (9.38%) 6	11 / 68 (16.18%) 11	12 / 70 (17.14%) 15

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 October 2018	Amendment in Sweden only: it became apparent that no spermicides are available, therefore inclusion criterion #4 required updating

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported