Clinical trial results:
A randomised, double-blind, placebo-controlled, proof-of-mechanism phase 2 trial investigating the effect of quinagolide extended-release vaginal ring on reduction of lesions assessed by high-resolution magnetic resonance imaging in women with endometrioma, deep infiltrating endometriosis, and/or adenomyosis

Summary

EudraCT number	2018-000915-26
Trial protocol	DE DK IT
Global end of trial date	18 July 2021

Results information

Result version number	v1 (current)
This version publication date	07 July 2022
First version publication date	07 July 2022

Trial information

Trial identification

Sponsor protocol code	000295

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03749109
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ferring Pharmaceuticals A/S
Sponsor organisation address	International PharmaScience Center, Amager Strandvej 405, Kastrup, Denmark, 2770
Public contact	Global Clinical Compliance, Ferring Pharmaceuticals A/S, DK0-Disclosure@ferring.com
Scientific contact	Global Clinical Compliance, Ferring Pharmaceuticals A/S, 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	26 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2021
Global end of trial reached?	Yes
Global end of trial date	18 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of quinagolide vaginal ring compared to placebo on reduction of lesions for endometrioma, deep infiltrating endometriosis (DIE) and adenomyosis assessed by high-resolution magnetic resonance imaging (MRI)

Protection of trial subjects:

The trial was performed in compliance with International Council for Harmonisation (ICH) guideline on Good Clinical Practice (GCP)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 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	Denmark: 3
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Poland: 60
Worldwide total number of subjects	67
EEA total number of subjects	67

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)	67
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was performed in 6 investigational sites in 3 countries between Aug 2019 to Jul 2021.

Pre-assignment

Screening details:

In total, 147 subjects were screened. Of these, 80 were screening failures and 67 were randomized and exposed to the investigational medicinal product (IMP): 35 to Quinagolide and 32 to Placebo.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Quinagolide 1080 µg

Arm description:

Vaginal ring containing Quinagolide 1080 µg, with daily target release rate of 13.5 µg.

Quinagolide 1080 µg: Vaginal ring containing Quinagolide 1080 µg for daily releases

Arm type	Experimental
Investigational medicinal product name	Quinagolide 1080 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal delivery system
Routes of administration	Vaginal use

Dosage and administration details:

Vaginal ring containing Quinagolide 1080 µg, with daily target release rate of 13.5 µg.

Arm title	Placebo

Arm description:

Vaginal ring containing matching placebo

Placebo: Matching placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal delivery system
Routes of administration	Vaginal use

Dosage and administration details:

Vaginal ring containing matching placebo

Number of subjects in period 1	Quinagolide 1080 µg	Placebo
Started	35	32
Completed	33	32
Not completed	2	0
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups

Reporting group title	Quinagolide 1080 µg

Reporting group description:

Vaginal ring containing Quinagolide 1080 µg, with daily target release rate of 13.5 µg.

Quinagolide 1080 µg: Vaginal ring containing Quinagolide 1080 µg for daily releases

Reporting group title	Placebo

Reporting group description:

Vaginal ring containing matching placebo

Placebo: Matching placebo

Reporting group values	Quinagolide 1080 µg	Placebo	Total
Number of subjects	35	32	67
Age categorical Units: Subjects			
Adults (18-64 years)	35	32	67
Age continuous Units: years			
arithmetic mean	36.9	35.2	
standard deviation	± 5.51	± 5.96	-
Gender categorical Units: Subjects			
Female	35	32	67
Male	0	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	35	32	67
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
White	34	32	66
Body Mass Index (BMI) Units: kg/m^2			
arithmetic mean	23.91	23.30	
standard deviation	± 3.86	± 4.15	-

Subject analysis sets

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All analyses for primary and secondary efficacy endpoints are presented by lesion type. This means one subject can be included in multiple lesion groups, depending on the type of lesion(s) with a size of ≥10 mm present at baseline. Thus, the FAS population by lesion type includes 47 subjects in the endometrioma group, 45 subjects in the DIE group, and 36 subjects in the adenomyosis group. The primary and secondary efficacy results are presented for these subjects unless otherwise specified.

The FAS comprised all randomised and exposed subjects according to the planned treatment; this included 35 subjects in the quinagolide vaginal ring group and 32 subjects in the placebo vaginal ring group.
The FAS by each lesion type is primarily used for presenting the efficacy results.

Reporting group values	Full analysis set (FAS)		
Number of subjects	67		
Age categorical Units: Subjects			
Adults (18-64 years)			
Age continuous Units: years			
arithmetic mean	36.1		
standard deviation	± 5.75		
Gender categorical Units: Subjects			
Female			
Male			
Ethnicity Units: Subjects			
Not Hispanic or Latino			
Race Units: Subjects			
American Indian or Alaska Native			
White			
Body Mass Index (BMI) Units: kg/m^2			
arithmetic mean	23.62		
standard deviation	± 3.98		

End points

End points reporting groups

Reporting group title	Quinagolide 1080 µg

Reporting group description:

Vaginal ring containing Quinagolide 1080 µg, with daily target release rate of 13.5 µg.

Quinagolide 1080 µg: Vaginal ring containing Quinagolide 1080 µg for daily releases

Reporting group title	Placebo

Reporting group description:

Vaginal ring containing matching placebo

Placebo: Matching placebo

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All analyses for primary and secondary efficacy endpoints are presented by lesion type. This means one subject can be included in multiple lesion groups, depending on the type of lesion(s) with a size of ≥10 mm present at baseline. Thus, the FAS population by lesion type includes 47 subjects in the endometrioma group, 45 subjects in the DIE group, and 36 subjects in the adenomyosis group. The primary and secondary efficacy results are presented for these subjects unless otherwise specified.

The FAS comprised all randomised and exposed subjects according to the planned treatment; this included 35 subjects in the quinagolide vaginal ring group and 32 subjects in the placebo vaginal ring group.
The FAS by each lesion type is primarily used for presenting the efficacy results.

Primary: Changes in the Sizes (mm) of Endometrioma, Deep Infiltrating Endometriosis (DIE) and Adenomyosis Lesions Summed by Type on Magnetic Resonance (MR) Images at Cycle 4

End point title	Changes in the Sizes (mm) of Endometrioma, Deep Infiltrating Endometriosis (DIE) and Adenomyosis Lesions Summed by Type on Magnetic Resonance (MR) Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

At screening, every measurable lesion (defined as ≥10 mm in size) of any type was recorded and was summed up by type for primary analysis.

End point type	Primary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=25), DIE (n=19), Adenomyosis (n=20)
Placebo: Endometrioma (n=22), DIE (n=26), Adenomyosis (n=16)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: mm				
least squares mean (standard error)				
Endometrioma	-0.20 (± 4.34)	-1.94 (± 4.48)		

DIE Adenomyosis	2.41 (± 2.52) -3.10 (± 3.75)	-0.94 (± 2.03) -3.43 (± 3.87)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.78
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.45
upper limit	13.94
Variability estimate	Standard error of the mean

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.29
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	3.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.89
upper limit	9.59
Variability estimate	Standard error of the mean

Statistical analysis title	Quinagolide 1080 µg, Placebo

Statistical analysis description:	
Adenomyosis	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.95
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.33
upper limit	10.99
Variability estimate	Standard error of the mean

Secondary: Percentage of Changes in the Sizes of Endometrioma, DIE and Adenomyosis Lesions Summed by Type on MR Images at Cycle 4

End point title	Percentage of Changes in the Sizes of Endometrioma, DIE and Adenomyosis Lesions Summed by Type on MR Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=22), DIE (n=17), Adenomyosis (n=17)
Placebo: Endometrioma (n=21), DIE (n=25), Adenomyosis (n=16)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Percentage of changes in the size				
arithmetic mean (standard deviation)				
Endometrioma	15.64 (± 70.12)	-6.83 (± 44.46)		
DIE	7.67 (± 15.22)	5.81 (± 37.73)		
Adenomyosis	-3.04 (± 32.31)	-6.99 (± 25.48)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma	
Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.65
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-6.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.8
upper limit	22.82
Variability estimate	Standard error of the mean

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE	
Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.92
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.77
upper limit	20.51
Variability estimate	Standard error of the mean

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis	
Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.74
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-5.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.94
upper limit	29.1
Variability estimate	Standard error of the mean

Secondary: Proportion of Lesions by Type With a Decrease in a Size of ≥5 mm on MR Images at Cycle 4

End point title	Proportion of Lesions by Type With a Decrease in a Size of ≥5 mm on MR Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=53), DIE (n=26), Adenomyosis (n=33)
Placebo: Endometrioma (n=46), DIE (n=33), Adenomyosis (n=29)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Percentage of lesions				
number (not applicable)				
Endometrioma	18.9	21.7		
DIE	0	12.1		
Adenomyosis	12.1	24.1		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo

Statistical analysis description:

Endometrioma

Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.95
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	2.82

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description:	
Adenomyosis	
Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.39
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	2.17

Secondary: Proportion of Subjects With a Lesion of Any Type Decreased in a Size of ≥5 mm on MR Images at Cycle 4

End point title	Proportion of Subjects With a Lesion of Any Type Decreased in a Size of ≥5 mm on MR Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=25), DIE (n=19), Adenomyosis (n=20)
Placebo: Endometrioma (n=22), DIE (n=26), Adenomyosis (n=16)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Percentage of subjects				
number (not applicable)				
Endometrioma	24.0	31.8		
DIE	0	11.5		
Adenomyosis	15.0	37.5		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	2.65

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.21
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	1.79

Secondary: Number of New or Disappearing Endometrioma, DIE and Adenomyosis Lesions Summed by Type on MR Images at Cycle 4

End point title	Number of New or Disappearing Endometrioma, DIE and Adenomyosis Lesions Summed by Type on MR Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Lesions				
number (not applicable)				
Endometrioma - Disappearing Lesions	14	5		
DIE - Disappearing Lesions	0	1		
Adenomyosis - Disappearing Lesions	1	2		
Endometrioma - New Lesions	3	3		
DIE - New Lesions	0	0		
Adenomyosis - New Lesions	0	0		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo

Statistical analysis description:

Endometrioma - Disappearing Lesions

Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.13
Method	Negative-binomial regression
Parameter estimate	Rate Ratio
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	8.39

Statistical analysis title	Quinagolide 1080 µg, Placebo
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.56
Method	Negative-binomial regression
Parameter estimate	Rate Ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	5.41

Secondary: Changes in the Volumes (mm3) of Endometrioma and DIE Lesions Summed by Type on MR Images at Cycle 4

End point title	Changes in the Volumes (mm3) of Endometrioma and DIE Lesions Summed by Type on MR Images at Cycle 4

End point description:

The MRI examination was performed on a high resolution 3T machine at screening and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=25), DIE (n=19)
Placebo: Endometrioma (n=22), DIE (n=26)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: mm3				
least squares mean (standard error)				
Endometrioma	2.12 (± 4.62)	1.89 (± 4.77)		
DIE	-0.15 (± 1.81)	-0.87 (± 1.25)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description:	
Endometrioma	
Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.97
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.78
upper limit	13.23
Variability estimate	Standard error of the mean

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description:	
DIE	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.74
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.63
upper limit	5.07
Variability estimate	Standard error of the mean

Secondary: Changes in the Sizes of Endometrioma Assessed by Transvaginal Ultrasound (TVU) at Cycle 4

End point title	Changes in the Sizes of Endometrioma Assessed by Transvaginal Ultrasound (TVU) at Cycle 4

End point description:

Transvaginal ultrasound (TVU) will be performed, preferably by the same sonographer, at the screening visit and at end-of-treatment / cycle 4.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 4 months, each cycle is approximately 28 days)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: mm				
least squares mean (standard error)				
Endometrioma	14.19 (± 8.70)	4.06 (± 9.02)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.42
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	10.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.74
upper limit	35
Variability estimate	Standard error of the mean

Secondary: Changes in the Mean Individual and Total Symptom and Sign Severity of Scores of the Biberoglu and Behrman (B&B) Scale at Cycle 4

End point title	Changes in the Mean Individual and Total Symptom and Sign Severity of Scores of the Biberoglu and Behrman (B&B) Scale at Cycle 4

End point description:

B&B scale is a used scale for endometriosis that consists of two parts, with the first part evaluating symptoms (i.e. different types of pain) and the second part evaluating physical signs.
B&B scale is a 4-point scale with 0=none and 3=severe.

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 4 months, each cycle is approximately 28 days)

Quinagolide 1080 µg: Endometrioma (n=24), DIE (n=19), Adenomyosis (n=20)
Placebo: Endometrioma (n=22), DIE (n=26), Adenomyosis (n=16)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Change of score of B&B scale				
least squares mean (standard deviation)				
Endometrioma	-1.2 (± 2.26)	-2.1 (± 2.51)		
DIE	-1.3 (± 2.16)	-1.6 (± 2.21)		
Adenomyosis	-1.5 (± 2.33)	-1.9 (± 1.86)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma	
Comparison groups	Placebo v Quinagolide 1080 µg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.38

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.67
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	1.58

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description:	
Adenomyosis	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.64
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	1.71

Secondary: Changes in the Numerical Rating Scale (NRS) Pain Scores Per Cycle at Cycles 1, 2, 3 and 4

End point title	Changes in the Numerical Rating Scale (NRS) Pain Scores Per Cycle at Cycles 1, 2, 3 and 4

End point description:

Assessed by participants. NRS is a 11-point scale, with 0 indicating no pain and 10 indicating the worst imaginable pain

Quinagolide 1080 µg: Endometrioma (n=24), DIE (n=19)
Adenomyosis cycle 1 (n=20), cycle 2 (n=20), cycle 3 (n=19), cycle 4 (n=20)

Placebo: Endometrioma (n=22), DIE (n=26), Adenomyosis (n=16)

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycles 1 (~1 month), 2 (~2 months), 3 (~3 months) and 4 (~4 months)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: score on a scale				
least squares mean (standard deviation)				
Endometrioma at cycle 1	-0.5 (± 1.96)	-0.7 (± 2.21)		
Endometrioma at cycle 2	-0.9 (± 2.17)	-1.1 (± 2.85)		

Endometrioma at cycle 3	-1.7 (± 2.73)	-1.1 (± 1.67)		
Endometrioma at cycle 4	-1.5 (± 3.11)	-2.0 (± 1.94)		
DIE at cycle 1	-0.6 (± 2.14)	-0.7 (± 2.19)		
DIE at cycle 2	-1.1 (± 2.20)	-1.4 (± 2.97)		
DIE at cycle 3	-1.7 (± 2.65)	-1.0 (± 1.97)		
DIE at cycle 4	-1.2 (± 2.27)	-2.1 (± 2.21)		
Adenomyosis at cycle 1	0.3 (± 1.84)	-0.7 (± 2.24)		
Adenomyosis at cycle 2	-0.7 (± 2.37)	-0.9 (± 2.13)		
Adenomyosis at cycle 3	-0.8 (± 2.34)	-0.9 (± 1.78)		
Adenomyosis at cycle 4	-1.6 (± 2.91)	-1.9 (± 2.28)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma at cycle 1	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.73
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	1.44

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma at cycle 2	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.54
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	1.82

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma at cycle 3	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.46
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	0.85

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.49
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	2.05

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 1	
Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.99
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.32
upper limit	1.3

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 2	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.83
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	1.71

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 3	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.28
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	0.63

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.26
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	2.07

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 1	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.19
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	2.31

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 2	
Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.93
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	1.58

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 3	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.85
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	1.32

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.99
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	1.69

Secondary: Changes in the Endometriosis Health Profile-30 (EHP-30) Scores at Cycles 2 and 4

End point title	Changes in the Endometriosis Health Profile-30 (EHP-30) Scores at Cycles 2 and 4

End point description:

EHP-30 is a quality-of-life questionnaire. Score ranges from 0-100 and lower score denotes improvement.

It consists of 30 questions measuring the frequency of the endometriosis impact on their quality of life during the past four weeks, with five options of never, rarely, sometimes, often and always.

End point type	Secondary

End point timeframe:

At baseline, at menstrual cycles 2 (~2 months) and 4 (~4 months)

Quinagolide 1080 µg: Endometrioma (n=24), DIE (n=19), Adenomyosis (n=20)
Placebo: Endometrioma (n=22), DIE (n=26), Adenomyosis (n=16)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Score on a scale				
least squares mean (standard deviation)				
Endometrioma at cycle 2	-46.6 (± 90.49)	-51.0 (± 71.60)		
Endometrioma at cycle 4	-56.6 (± 88.84)	-94.0 (± 85.14)		
DIE at cycle 2	-55.6 (± 91.14)	-41.7 (± 86.27)		
DIE at cycle 4	-54.8 (± 87.29)	-85.7 (± 98.96)		
Adenomyosis at cycle 2	-46.3 (± 102.92)	-33.2 (± 52.21)		
Adenomyosis at cycle 4	-64.9 (± 105.62)	-79.4 (± 90.04)		

Statistical analyses

Statistical analysis title	Quinagolide 1080 µg, Placebo

Statistical analysis description:

Endometrioma at cycle 2

Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.75
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-7.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.97
upper limit	39.27

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Endometrioma at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.42
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	17.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.41
upper limit	60.04

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 2	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.47
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-17.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.3
upper limit	30.98

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: DIE at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.27
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	25.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.05
upper limit	72.27

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 2	
Comparison groups	Quinagolide 1080 µg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.41
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-20.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.83
upper limit	29.92

Statistical analysis title	Quinagolide 1080 µg, Placebo
Statistical analysis description: Adenomyosis at cycle 4	
Comparison groups	Quinagolide 1080 µg v Placebo

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.93
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.57
upper limit	54.06

Secondary: Changes in the Menstrual Bleeding Pattern Over 4 Cycles

End point title	Changes in the Menstrual Bleeding Pattern Over 4 Cycles

End point description:

Assessed by patient self-reported answers to menstrual bleeding questions.
The Menstrual Bleeding Pattern covered the Menstrual Cycle Duration and the Menstrual Bleeding Duration.

Menstrual Cycle Duration:
Quinagolide 1080 µg: Endometrioma cycle(C) 1 (n=23), C2 (n=24), C3 (n=22), C4 (n=23), DIE C1 (n=18), C2 (n=18), C3 (n=17), C4 (n=19), Adenomyosis C1 (n=19), C2 (n=19), C3 (n=16), C4 (n=18).
Placebo: Endometrioma C1 (n=22), C2 (n=22), C3 (n=23), C4 (n=23), DIE C1 (n=26), C2 (n=26), C3 (n=27), C4 (n=26), Adenomyosis C1 (n=16), C2 (n=16), C3 (n=17), C4 (n=17).

Menstrual Bleeding Duration:
Quinagolide 1080 µg: Endometrioma C1 (n=24), C2 (n=25), C3 (n=24), C4 (n=26), DIE C1 (n=19), C2 (n=20), C3 (n=19), C4 (n=20), Adenomyosis C1 (n=19), C2 (n=19), C3 (n=16), C4 (n=18).
Placebo: Endometrioma C1 (n=22), C2 (n=22), C3 (n=23), C4 (n=24), DIE C1 (n=26), C2 (n=26), C3 (n=27), C4 (n=27), Adenomyosis C1 (n=16), C2 (n=16), C3 (n=17), C4 (n=17).

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycles 1 (~1 month), 2 (~2 months), 3 (~3 months) and 4 (~4 months)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Days				
arithmetic mean (standard deviation)				
Endometrioma at baseline (cycle duration)	31.9 (± 10.54)	32.6 (± 10.38)		
Endometrioma at cycle 1 (cycle duration)	27.8 (± 2.92)	26.9 (± 2.39)		
Endometrioma at cycle 2 (cycle duration)	28.1 (± 2.13)	27.4 (± 2.50)		
Endometrioma at cycle 3 (cycle duration)	27.7 (± 2.12)	28.3 (± 2.65)		

Endometrioma at cycle 4 (cycle duration)	28.2 (± 3.27)	26.9 (± 2.23)		
DIE at baseline (cycle duration)	33.2 (± 11.80)	31.4 (± 9.45)		
DIE at cycle 1 (cycle duration)	26.7 (± 2.66)	27.3 (± 2.78)		
DIE at cycle 2 (cycle duration)	27.4 (± 1.98)	27.7 (± 2.52)		
DIE at cycle 3 (cycle duration)	28.2 (± 2.86)	28.5 (± 2.29)		
DIE at cycle 4 (cycle duration)	26.9 (± 2.23)	27.7 (± 2.59)		
Adenomyosis at baseline (cycle duration)	33.5 (± 11.16)	32.4 (± 11.49)		
Adenomyosis at cycle 1 (cycle duration)	27.7 (± 2.54)	26.8 (± 2.61)		
Adenomyosis at cycle 2 (cycle duration)	28.3 (± 2.23)	27.4 (± 2.37)		
Adenomyosis at cycle 3 (cycle duration)	27.8 (± 2.52)	27.9 (± 1.93)		
Adenomyosis at cycle 4 (cycle duration)	27.2 (± 1.50)	27.4 (± 1.87)		
Endometrioma at baseline (bleeding duration)	5.1 (± 1.08)	5.1 (± 0.97)		
Endometrioma at cycle 1 (bleeding duration)	5.3 (± 1.71)	4.7 (± 0.77)		
Endometrioma at cycle 2 (bleeding duration)	5.3 (± 1.22)	5.1 (± 0.87)		
Endometrioma at cycle 3 (bleeding duration)	4.5 (± 1.61)	4.8 (± 0.89)		
Endometrioma at cycle 4 (bleeding duration)	5.0 (± 1.43)	4.7 (± 1.52)		
DIE at baseline (bleeding duration)	4.9 (± 0.99)	5.3 (± 1.01)		
DIE at cycle 1 (bleeding duration)	5.0 (± 1.60)	4.6 (± 0.70)		
DIE at cycle 2 (bleeding duration)	5.0 (± 1.82)	5.0 (± 1.04)		
DIE at cycle 3 (bleeding duration)	4.5 (± 1.22)	4.9 (± 0.93)		
DIE at cycle 4 (bleeding duration)	5.2 (± 1.04)	4.9 (± 1.60)		
Adenomyosis at baseline (bleeding duration)	5.2 (± 1.20)	5.4 (± 1.15)		
Adenomyosis at cycle 1 (bleeding duration)	5.0 (± 1.75)	4.9 (± 0.62)		
Adenomyosis at cycle 2 (bleeding duration)	4.6 (± 1.78)	4.8 (± 1.17)		
Adenomyosis at cycle 3 (bleeding duration)	4.3 (± 1.66)	4.7 (± 1.05)		
Adenomyosis at cycle 4 (bleeding duration)	5.0 (± 0.74)	5.0 (± 1.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Levels of Prolactin During Cycle 1, at Cycles 2 and 4

End point title	Serum Levels of Prolactin During Cycle 1, at Cycles 2 and 4

End point description:

Assessed by blood sample collection

Quinagolide 1080 µg: Endometrioma at cycle 1 (n=24), Endometrioma at cycle 2 (n=24), Endometrioma at cycle 4 (n=25), DIE at cycle 1 (n=19), DIE at cycle 2 (n=19), DIE at cycle 4 (n=19), Adenomyosis at cycle 1 (n=20), Adenomyosis at cycle 2 (n=20), Adenomyosis at cycle 4 (n=20).

Placebo: Endometrioma at cycle 1 (n=21), Endometrioma at cycle 2 (n=22), Endometrioma at cycle 4 (n=22), DIE at cycle 1 (n=25), DIE at cycle 2 (n=26), DIE at cycle 4 (n=26), Adenomyosis at cycle 1 (n=15), Adenomyosis at cycle 2 (n=16), Adenomyosis at cycle 4 (n=16)

End point type	Secondary

End point timeframe:

Within 1-5 days post randomisation, and at menstrual cycles 2 (~2 months) and 4 (~4 months)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: pg/L				
least squares mean (standard deviation)				
Endometrioma at cycle 1	5.51 (± 3.604)	12.68 (± 4.618)		
Endometrioma at cycle 2	9.30 (± 4.739)	12.79 (± 4.381)		
Endometrioma at cycle 4	9.47 (± 4.081)	12.31 (± 6.648)		
DIE at cycle 1	5.95 (± 3.258)	10.80 (± 4.201)		
DIE at cycle 2	10.36 (± 5.118)	11.85 (± 5.029)		
DIE at cycle 4	10.65 (± 4.465)	12.08 (± 6.739)		
Adenomyosis at cycle 1	5.80 (± 4.017)	12.13 (± 4.563)		
Adenomyosis at cycle 2	7.97 (± 2.608)	11.94 (± 4.150)		
Adenomyosis at cycle 4	9.35 (± 3.418)	11.95 (± 4.395)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Levels of Thyroid-stimulating Hormone (TSH) During Cycle 1, at Cycles 2 and 4

End point title	Serum Levels of Thyroid-stimulating Hormone (TSH) During Cycle 1, at Cycles 2 and 4

End point description:

Assessed by blood sample collection

Quinagolide 1080 µg: Endometrioma at cycle 1 (n=24), Endometrioma at cycle 2 (n=24), Endometrioma at cycle 4 (n=25), DIE at cycle 1 (n=19), DIE at cycle 2 (n=19), DIE at cycle 4 (n=19), Adenomyosis at cycle 1 (n=20), Adenomyosis at cycle 2 (n=20), Adenomyosis at cycle 4 (n=20).

Placebo: Endometrioma at cycle 1 (n=21), Endometrioma at cycle 2 (n=22), Endometrioma at cycle 4 (n=22), DIE at cycle 1 (n=25), DIE at cycle 2 (n=26), DIE at cycle 4 (n=26), Adenomyosis at cycle 1 (n=15), Adenomyosis at cycle 2 (n=16), Adenomyosis at cycle 4 (n=16)

End point type	Secondary

End point timeframe:

Within 1-5 days post randomisation, and at menstrual cycles 2 (~2 months) and 4 (~4 months)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: mIU/L				
arithmetic mean (standard deviation)				
Endometrioma at cycle 1	1.672 (± 1.3376)	1.513 (± 0.6822)		
Endometrioma at cycle 2	1.785 (± 1.0535)	1.509 (± 0.6746)		
Endometrioma at cycle 4	1.692 (± 0.9489)	1.422 (± 0.6528)		
DIE at cycle 1	1.706 (± 1.5550)	1.394 (± 0.8200)		
DIE at cycle 2	1.726 (± 1.1633)	1.383 (± 0.6903)		
DIE at cycle 4	1.375 (± 0.8953)	1.299 (± 0.6571)		
Adenomyosis at cycle 1	2.067 (± 1.8100)	1.325 (± 0.7248)		
Adenomyosis at cycle 2	1.722 (± 1.1557)	1.311 (± 0.5664)		
Adenomyosis at cycle 4	1.801 (± 0.9463)	1.353 (± 0.5614)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Levels of Insulin-like Growth Factor-1 (IGF-1) During Cycle 1, at Cycles 2 and 4

End point title	Serum Levels of Insulin-like Growth Factor-1 (IGF-1) During Cycle 1, at Cycles 2 and 4

End point description:

Assessed by blood sample collection

Quinagolide 1080 µg: Endometrioma at cycle 1 (n=24), Endometrioma at cycle 2 (n=23), Endometrioma at cycle 4 (n=25), DIE at cycle 1 (n=19), DIE at cycle 2 (n=19), DIE at cycle 4 (n=19), Adenomyosis at cycle 1 (n=20), Adenomyosis at cycle 2 (n=19), Adenomyosis at cycle 4 (n=20).

Placebo: Endometrioma at cycle 1 (n=21), Endometrioma at cycle 2 (n=22), Endometrioma at cycle 4 (n=22), DIE at cycle 1 (n=25), DIE at cycle 2 (n=26), DIE at cycle 4 (n=26), Adenomyosis at cycle 1 (n=15), Adenomyosis at cycle 2 (n=16), Adenomyosis at cycle 4 (n=16)

End point type	Secondary

End point timeframe:

Within 1-5 days post randomisation, and at menstrual cycles 2 (~2 months) and 4 (~4 months)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: nmol/L				
arithmetic mean (standard deviation)				
Endometrioma at cycle 1	23.90 (± 8.002)	22.96 (± 6.721)		
Endometrioma at cycle 2	19.9 (± 6.511)	21.81 (± 5.481)		
Endometrioma at cycle 4	21.82 (± 5.450)	20.22 (± 5.786)		
DIE at cycle 1	22.16 (± 8.099)	23.68 (± 6.135)		
DIE at cycle 2	18.01 (± 5.484)	21.07 (± 6.526)		
DIE at cycle 4	20.98 (± 5.678)	20.53 (± 6.083)		
Adenomyosis at cycle 1	21.80 (± 7.763)	22.51 (± 4.580)		
Adenomyosis at cycle 2	19.17 (± 6.497)	19.93 (± 5.233)		
Adenomyosis at cycle 4	21.19 (± 6.331)	18.93 (± 4.836)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Quinagolide and Its Metabolites During Cycles 1 to 4

End point title	Plasma Concentrations of Quinagolide and Its Metabolites During Cycles 1 to 4[1]

End point description:

Assessed by blood sample collection.

Quinagolide 1080 µg: Within 1-5 days of randomisation (n=30), Within 7-14 days of randomisation (n=32), Cycle 1 (n=32), Cycle 2 (n=33), Cycle 3 (n=32), Cycle 4 (n=32)

End point type	Secondary

End point timeframe:

Within 1-5 days post randomisation, within 7-14 days post randomisation, and at menstrual cycles 1 (~1 months), 2 (~2 months), 3 (~3 months) and 4 (~4 months)

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: The endpoint measured the plasma concentration of Quinagolide and its metabolites. You cannot measure the plasma concentration of quinagolide for the subjects who have received placebo.

End point values	Quinagolide 1080 µg			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: pg/mL				
arithmetic mean (standard deviation)				
Within 1-5 days of randomisation	11.66 (± 5.23)			

Within 7-14 days of randomisation	5.50 (± 2.59)			
Cycle 1	2.90 (± 1.33)			
Cycle 2	2.92 (± 1.68)			
Cycle 3	2.78 (± 1.32)			
Cycle 4	3.16 (± 3.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Clinical Chemistry and Hematology Parameters

End point title	Changes in Clinical Chemistry and Hematology Parameters

End point description:

Assessed by blood sample collection

The parameters have different units.
Hematocrit: % v/v
Hemaglobin: g/L
Ery. Mean Corpuscular Hemoglobin: pg/cell
Ery. Mean Corpuscular HGB Concentration: g/L
Ery. Mean Corpuscular Volume: fL
Platelets: 10^9/L
Erythrocytes: 10^12/L
Leukocytes: 10^9/L
Alanine Aminotransferase: U/L
Albumin: g/L
Alkaline Phosphatase: IU/L
Aspartate Aminotransferase: U/L
Bicarbonate: mmol/L
Direct Bilirubin: umol/L
Bilirubin: umol/L
Calcium: mmol/L
Chloride: mmol/L
Cholesterol: mmol/L
Creatinine: umol/L
Gamma Glutamyl Transferase: U/L
Glucose: mmol/L
Lactate Dehydrogenase: U/L
Phosphate: mmol/L
Potassium: mmol/L
Sodium: mmol/L
Protein: g/L
Urate: umol/L
Urea Nitrogen: mmol/L

End point type	Secondary

End point timeframe:

At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: % v/v				
arithmetic mean (standard deviation)				

Hematocrit	-0.007 (± 0.0181)	-0.005 (± 0.0259)		
Hemaglobin	-3.6 (± 5.60)	-3.2 (± 8.69)		
Ery. mean Corpuscular Hemoglobin	-0.7 (± 0.71)	-0.6 (± 1.22)		
Ery. Mean Corpuscular HGB Concentration	-3.1 (± 7.11)	-4.3 (± 8.76)		
Ery. Mean Corpuscular Volume	-1.2 (± 2.11)	-0.7 (± 3.10)		
Platelets	4.9 (± 33.98)	11.6 (± 45.92)		
Erythrocytes	-0.02 (± 0.192)	-0.01 (± 0.228)		
Leukocytes	-0.43 (± 1.928)	0.18 (± 2.055)		
Alanine Aminotransferase	-1.1 (± 5.88)	-0.2 (± 3.86)		
Albumin	0.0 (± 2.28)	0.7 (± 2.84)		
Alkaline Phosphatase	3.1 (± 8.18)	4.2 (± 6.67)		
Aspartate Aminotransferase	1.0 (± 3.72)	0.5 (± 3.43)		
Bicarbonate	-2.7 (± 2.59)	-2.9 (± 2.51)		
Direct Bilirubin	0.0 (± 0.38)	0.0 (± 1.10)		
Bilirubin	-1.2 (± 2.84)	-0.8 (± 4.57)		
Calcium	0.009 (± 0.0896)	0.012 (± 0.0773)		
Chloride	0.2 (± 2.68)	-0.5 (± 2.49)		
Cholesterol	0.045 (± 0.5050)	0.244 (± 0.5219)		
Creatinine	-3.5 (± 8.21)	-4.3 (± 7.82)		
Gamma Glutamyl Transferase	-1.1 (± 4.77)	1.0 (± 4.46)		
Glucose	-0.07 (± 0.734)	-0.06 (± 0.866)		
Lactate Dehydrogenase	2.7 (± 12.30)	2.8 (± 8.42)		
Phosphate	-0.013 (± 0.1452)	0.048 (± 0.1885)		
Potassium	0.07 (± 0.333)	0.06 (± 0.357)		
Sodium	0.7 (± 2.04)	0.4 (± 2.54)		
Protein	-0.1 (± 3.82)	1.4 (± 3.19)		
Urate	10.7 (± 56.36)	1.3 (± 37.59)		
Urea Nitrogen	-0.180 (± 1.0184)	0.148 (± 1.2286)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects With Markedly Abnormal Changes in Clinical Chemistry and Hematology Parameters

End point title	Proportion of Subjects With Markedly Abnormal Changes in Clinical Chemistry and Hematology Parameters
End point description:	
Assessed by blood sample collection	
End point type	Secondary
End point timeframe:	
At baseline and at menstrual cycle 4 (around 5 months, each cycle is approximately 28 days)	

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Percentage of subjects				
number (not applicable)	2.86	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and Intensity of Adverse Events

End point title	Frequency and Intensity of Adverse Events

End point description:

Assessed by and Adverse Event Log completed by the Investigator

End point type	Secondary

End point timeframe:

From obtaining the informed consent to end of trial (up to 6 menstrual cycles ~ around 6 months, each cycle is approximately 28 days)

End point values	Quinagolide 1080 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: Percentage of adverse events				
number (not applicable)				
Mild adverse events	28.6	43.8		
Moderate adverse events	42.9	37.5		
Severe adverse events	2.9	9.4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time of signed informed consent for participation in the trial to end-of-trial.

Adverse event reporting additional description:

All adverse events with onset after start of first administration of IMP and before the follow-up phone call were considered treatment-emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Quinagolide 1080 µg

Reporting group description:

Vaginal ring containing Quinagolide 1080 µg, with daily target release rate of 13.5 µg.

Quinagolide 1080 µg: Vaginal ring containing Quinagolide 1080 µg for daily releases

Reporting group title	Placebo

Reporting group description:

Vaginal ring containing matching placebo

Placebo: Matching placebo

Serious adverse events	Quinagolide 1080 µg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 35 (2.86%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Quinagolide 1080 µg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 35 (57.14%)	20 / 32 (62.50%)	

Vascular disorders Hot flush subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	0 / 32 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1 6 / 35 (17.14%) 9 0 / 35 (0.00%) 0 2 / 35 (5.71%) 4	4 / 32 (12.50%) 4 8 / 32 (25.00%) 15 2 / 32 (6.25%) 2 1 / 32 (3.13%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Peripheral swelling subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1 2 / 35 (5.71%) 2 2 / 35 (5.71%) 5	2 / 32 (6.25%) 2 1 / 32 (3.13%) 1 0 / 32 (0.00%) 0	
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Rectal Haemorrhage	2 / 35 (5.71%) 2 3 / 35 (8.57%) 3	1 / 32 (3.13%) 1 2 / 32 (6.25%) 3	

subjects affected / exposed	0 / 35 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	4	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	2 / 35 (5.71%)	1 / 32 (3.13%)	
occurrences (all)	2	1	
Vulvovaginal pruritus			
subjects affected / exposed	2 / 35 (5.71%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Corona virus infection			
subjects affected / exposed	0 / 35 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)	1 / 32 (3.13%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported