



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 | 2.41 (\pm 2.52) | -0.94 (\pm 2.03) | | |
| Adenomyosis | -3.10 (\pm 3.75) | -3.43 (\pm 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

Hemoglobin: g/L

Ery. Mean Corpuscular Hemoglobin: pg/cell

Ery. Mean Corpuscular HGB Concentration: g/L

Ery. Mean Corpuscular Volume: fL

Platelets: 10⁹/L

Erythrocytes: 10¹²/L

Leukocytes: 10⁹/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 | 2 / 35 (5.71%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 4 / 32 (12.50%) | |
| occurrences (all) | 1 | 4 | |
| Headache | | | |
| subjects affected / exposed | 6 / 35 (17.14%) | 8 / 32 (25.00%) | |
| occurrences (all) | 9 | 15 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 35 (0.00%) | 2 / 32 (6.25%) | |
| occurrences (all) | 0 | 2 | |
| Somnolence | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 1 / 32 (3.13%) | |
| occurrences (all) | 4 | 1 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 35 (2.86%) | 2 / 32 (6.25%) | |
| occurrences (all) | 1 | 2 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 1 / 32 (3.13%) | |
| occurrences (all) | 2 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 0 / 32 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 35 (5.71%) | 1 / 32 (3.13%) | |
| occurrences (all) | 2 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 35 (8.57%) | 2 / 32 (6.25%) | |
| occurrences (all) | 3 | 3 | |
| Rectal Haemorrhage | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 35 (0.00%) 0 | 2 / 32 (6.25%) 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