



Clinical trial results:

Multicenter, randomized, open-label, parallel-group study to evaluate user satisfaction with and tolerability of the low-dose levonorgestrel (LNG) intrauterine delivery system (IUS) with 12 µg LNG/day initial in vitro release rate (LCS12) in comparison to a combined oral contraceptive containing 30 µg ethinyl estradiol and 3 mg drospirenone (Yasmin®) in young nulliparous and parous women (18-29 years) over 18 months of use

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-020181-21 |
| Trial protocol | AT BE DE |
| Global end of trial date | 28 May 2014 |

Results information

| | |
|--------------------------------|--|
| Result version number | v3 (current) |
| This version publication date | 07 September 2017 |
| First version publication date | 10 May 2015 |
| Version creation reason | <ul style="list-style-type: none">• New data added to full data set Update to include data reported in CSR amendment |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY86-5028/13362 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01254292 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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 | 28 May 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 May 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate user satisfaction in young nulliparous and parous women (18-29 years of age) using LCS12 compared with young nulliparous and parous women using a combined oral contraceptive (COC) over a period of 18 months.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 06 January 2011 |
| 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 | Austria: 173 |
| Country: Number of subjects enrolled | Belgium: 101 |
| Country: Number of subjects enrolled | Germany: 171 |
| Country: Number of subjects enrolled | United States: 122 |
| Worldwide total number of subjects | 567 |
| EEA total number of subjects | 445 |

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) | 567 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 42 centers across 4 countries in Austria, Belgium, Germany and United States.

Pre-assignment

Screening details:

644 subjects were screened, of which 77 were screen failures and 567 were randomized, 282 subjects to LCS12 and 285 subjects to Yasmin. 279 subjects randomized to LCS12 while 281 subjects randomized to Yasmin received treatment and started comparative phase up to 18 months. 200 subjects randomized to LCS12 entered extension phase up to 36 months.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Comparative Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | No |
| Arm title | LCS12 (Jaydess, BAY86-5028) |

Arm description:

Subjects received LCS12 for 18 months with optional extension to 36 months.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Levonorgestrel |
| Investigational medicinal product code | BAY86-5028 |
| Other name | Skyla, Jaydess |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects received LCS12 for 18 months with optional extension to 36 months.

| | |
|------------------|--------------------------------|
| Arm title | EE30/DRSP (Yasmin, BAY86-5131) |
|------------------|--------------------------------|

Arm description:

Subjects received COC tablet Yasmin containing 30 microgram ethinyl estradiol (EE) and 3 milligram (mg) drospirenone (DRSP) for 18 months per 19 cycles.

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | EE30/DRSP (Yasmin) |
| Investigational medicinal product code | BAY86-5131 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles.

| Number of subjects in period 1 | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) |
|--------------------------------|-----------------------------|--------------------------------|
| Started | 282 | 285 |
| Subjects Received Treatment | 279 | 281 |
| Completed | 227 | 204 |
| Not completed | 55 | 81 |
| Consent withdrawn by subject | 20 | 21 |
| Protocol violation | 1 | 2 |
| Wish for pregnancy | 4 | 6 |
| Pregnancy | 2 | 6 |
| Adverse event | 25 | 25 |
| Lost to follow-up | 3 | 21 |

Period 2

| | |
|------------------------------|-----------------------|
| Period 2 title | LCS12 Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-----------------------------|
| Arm title | LCS12 (Jaydess, BAY86-5028) |
|-----------|-----------------------------|

Arm description:

Subjects received LCS12 for 18 months with optional extension to 36 months.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Levonorgestrel |
| Investigational medicinal product code | BAY86-5028 |
| Other name | Skyla, Jaydess |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects received LCS12 for 18 months with optional extension to 36 months.

| Number of subjects in period 2 | LCS12 (Jaydess, BAY86-5028) |
|--------------------------------|-----------------------------|
| Started | 200 |
| Completed | 163 |
| Not completed | 37 |
| Consent withdrawn by subject | 7 |
| Wish for pregnancy | 14 |
| Other unknown | 4 |

| | |
|-------------------|---|
| Pregnancy | 2 |
| Adverse event | 9 |
| Lost to follow-up | 1 |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Baseline Period |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | No |
| Arm title | LCS12 (Jaydess, BAY86-5028) |

Arm description:

Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Levonorgestrel |
| Investigational medicinal product code | BAY86-5028 |
| Other name | Skyla, Jaydess |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects received LCS12 for 18 months with optional extension to 36 months.

| | |
|------------------|--------------------------------|
| Arm title | EE30/DRSP (Yasmin, BAY86-5131) |
|------------------|--------------------------------|

Arm description:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period.

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | EE30/DRSP (Yasmin) |
| Investigational medicinal product code | BAY86-5131 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: All subjects randomized to the 2 treatment groups were included in Comparative Phase. Baseline Period was created only for publishing the baseline characteristics which were provided for the treated subjects.

| Number of subjects in period 3 | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) |
|---------------------------------------|--------------------------------|-----------------------------------|
| Started | 279 | 281 |
| Completed | 279 | 281 |

Baseline characteristics

Reporting groups^[1]

| | |
|-----------------------|-----------------------------|
| Reporting group title | LCS12 (Jaydess, BAY86-5028) |
|-----------------------|-----------------------------|

Reporting group description:

Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period.

| | |
|-----------------------|--------------------------------|
| Reporting group title | EE30/DRSP (Yasmin, BAY86-5131) |
|-----------------------|--------------------------------|

Reporting group description:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period.

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all randomized subjects were treated with study drugs. Hence, the worldwide number enrolled in the trial, which is the same as the number randomized, differs from the number of subjects reported in the baseline period.

| Reporting group values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | Total |
|---------------------------------------|-----------------------------|--------------------------------|-------|
| Number of subjects | 279 | 281 | 560 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 279 | 281 | 560 |
| Age continuous Units: years | | | |
| arithmetic mean | 23.7 | 23.9 | |
| standard deviation | ± 3 | ± 3 | - |
| Gender categorical Units: Subjects | | | |
| Female | 279 | 281 | 560 |
| Number of births Units: Subjects | | | |
| Zero | 216 | 206 | 422 |
| One | 39 | 49 | 88 |
| Two | 19 | 24 | 43 |
| Three | 4 | 2 | 6 |
| Four | 1 | 0 | 1 |

Subject analysis sets

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Full analysis set (FAS) |
|----------------------------|-------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

The FAS included all randomized subjects who received treatment (i.e., who took at least one tablet of Yasmin or who had a successful or unsuccessful insertion attempt of LCS12). All subjects in the FAS were analyzed according to the treatment they actually received. The FAS population comprised of 560 subjects, including 279 subjects randomized to LCS12 and 281 subjects randomized to Yasmin.

| Reporting group values | Full analysis set (FAS) | | |
|------------------------|-------------------------|--|--|
| Number of subjects | 560 | | |

| | | | |
|---|-------|--|--|
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | | | |
| Age continuous Units: years arithmetic mean standard deviation | \pm | | |
| Gender categorical Units: Subjects | | | |
| Female | 560 | | |
| Number of births Units: Subjects | | | |
| Zero One Two Three Four | | | |

End points

End points reporting groups

| | |
|--|--------------------------------|
| Reporting group title | LCS12 (Jaydess, BAY86-5028) |
| Reporting group description: Subjects received LCS12 for 18 months with optional extension to 36 months. | |
| Reporting group title | EE30/DRSP (Yasmin, BAY86-5131) |
| Reporting group description: Subjects received COC tablet Yasmin containing 30 microgram ethinyl estradiol (EE) and 3 milligram (mg) drospirenone (DRSP) for 18 months per 19 cycles. | |
| Reporting group title | LCS12 (Jaydess, BAY86-5028) |
| Reporting group description: Subjects received LCS12 for 18 months with optional extension to 36 months. | |
| Reporting group title | LCS12 (Jaydess, BAY86-5028) |
| Reporting group description: Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period. | |
| Reporting group title | EE30/DRSP (Yasmin, BAY86-5131) |
| Reporting group description: Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period. | |
| Subject analysis set title | Full analysis set (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The FAS included all randomized subjects who received treatment (i.e., who took at least one tablet of Yasmin or who had a successful or unsuccessful insertion attempt of LCS12). All subjects in the FAS were analyzed according to the treatment they actually received. The FAS population comprised of 560 subjects, including 279 subjects randomized to LCS12 and 281 subjects randomized to Yasmin. | |

Primary: Overall Satisfaction Rate at 18 Months (Last Observation Carried Forward, LOCF)

| | |
|--|--|
| End point title | Overall Satisfaction Rate at 18 Months (Last Observation Carried Forward, LOCF) ^[1] |
| End point description: Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate is the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question. | |
| End point type | Primary |
| End point timeframe: At 18 months | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not performed since descriptive statistical analysis was only planned for this endpoint.

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|----------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 274 ^[2] | 260 ^[3] | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 82.1 (77.1 to 86.5) | 81.9 (76.7 to 86.4) | | |

Notes:

[2] - FAS (only subjects with at least one assessment of the overall satisfaction rating)

[3] - FAS (only subjects with at least one assessment of the overall satisfaction rating)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 6 Months

| | |
|--|--|
| End point title | Overall Satisfaction Rating by the 5-Point Likert Item at 6 Months |
| End point description: Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question. | |
| End point type | Secondary |
| End point timeframe: At 6 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 273 ^[4] | 260 ^[5] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Very Satisfied | 60.4 | 48.1 | | |
| Satisfied | 27.5 | 35.8 | | |
| Neither satisfied nor dissatisfied | 7.3 | 9.6 | | |
| Dissatisfied | 1.8 | 6.2 | | |
| Very Dissatisfied | 2.9 | 0.4 | | |

Notes:

[4] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months)

[5] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 12 Months

| | |
|--|---|
| End point title | Overall Satisfaction Rating by the 5-Point Likert Item at 12 Months |
| End point description: Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question. | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At 12 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 253 ^[6] | 238 ^[7] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Very Satisfied | 66.8 | 45 | | |
| Satisfied | 22.9 | 44.1 | | |
| Neither satisfied nor dissatisfied | 5.9 | 5.9 | | |
| Dissatisfied | 4.3 | 3.8 | | |
| Very Dissatisfied | 0 | 1.3 | | |

Notes:

[6] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

[7] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 18 Months

| | |
|-----------------|---|
| End point title | Overall Satisfaction Rating by the 5-Point Likert Item at 18 Months |
|-----------------|---|

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At 18 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 235 ^[8] | 217 ^[9] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Very Satisfied | 64.3 | 52.5 | | |
| Satisfied | 25.1 | 37.8 | | |
| Neither satisfied nor dissatisfied | 6.4 | 6.9 | | |
| Dissatisfied | 3 | 2.8 | | |
| Very Dissatisfied | 1.3 | 0 | | |

Notes:

[8] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months)

[9] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at End of Study (EOS)

| | |
|-----------------|--|
| End point title | Overall Satisfaction Rating by the 5-Point Likert Item at End of Study (EOS) |
|-----------------|--|

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 ^[10] | 251 ^[11] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Very Satisfied | 58.6 | 46.6 | | |
| Satisfied | 23.5 | 35.1 | | |
| Neither satisfied nor dissatisfied | 8.6 | 9.6 | | |
| Dissatisfied | 5.6 | 7.6 | | |
| Very Dissatisfied | 3.7 | 1.2 | | |

Notes:

[10] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months/EOS)

[11] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months/EOS)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rate at 6 Months (LOCF)

| | |
|-----------------|--|
| End point title | Overall Satisfaction Rate at 6 Months (LOCF) |
|-----------------|--|

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction

rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At 6 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 273 ^[12] | 260 ^[13] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 87.9 | 83.8 | | |

Notes:

[12] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months or before)

[13] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months or before)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rate at 12 Months (LOCF)

| | |
|-----------------|---|
| End point title | Overall Satisfaction Rate at 12 Months (LOCF) |
|-----------------|---|

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At 12 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 274 ^[14] | 260 ^[15] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 84.3 | 83.8 | | |

Notes:

[14] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

[15] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study

Treatment

| | |
|-----------------|--|
| End point title | User Satisfaction – Acceptability of the Administration of Study Treatment |
|-----------------|--|

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without inconvenience/discomfort (I/D), acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|----------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 ^[16] | 250 ^[17] | | |
| Units: subjects | | | | |
| Acceptable without I/D | 153 | 186 | | |
| Acceptable with some I/D | 87 | 46 | | |
| Not acceptable with moderate I/D | 11 | 15 | | |
| Not acceptable with extreme I/D | 12 | 3 | | |

Notes:

[16] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[17] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Choices Upon Completion of the Study

| | |
|-----------------|--|
| End point title | User Satisfaction – Choices Upon Completion of the Study |
|-----------------|--|

End point description:

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 ^[18] | 248 ^[19] | | |
| Units: subjects | | | | |
| Continue with study treatment | 174 | 122 | | |
| Use a different hormonal contraceptive | 34 | 51 | | |

| | | | | |
|---|----|----|--|--|
| Use a different contraceptive method | 17 | 27 | | |
| Discontinue use of all types of contraceptive | 6 | 14 | | |
| No need for contraceptive at this time | 5 | 12 | | |
| Undecided | 27 | 22 | | |

Notes:

[18] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[19] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Amount of Menstrual Bleeding

| | |
|---|--|
| End point title | User Satisfaction – Amount of Menstrual Bleeding |
| End point description: The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase. | |
| End point type | Secondary |
| End point timeframe: At 18 months/EOS | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-----------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 260 ^[20] | 250 ^[21] | | |
| Units: subjects | | | | |
| Decreased | 80 | 35 | | |
| Not Changed | 163 | 207 | | |
| Increased | 17 | 8 | | |

Notes:

[20] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[21] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Satisfaction With Menstrual Bleeding Pattern

| | |
|---|--|
| End point title | User Satisfaction – Satisfaction With Menstrual Bleeding Pattern |
| End point description: The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase. | |
| End point type | Secondary |
| End point timeframe: At 18 months/EOS | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 ^[22] | 250 ^[23] | | |
| Units: subjects | | | | |
| Very satisfied | 101 | 91 | | |
| Somewhat satisfied | 65 | 84 | | |
| Neither satisfied nor dissatisfied | 48 | 68 | | |
| Dissatisfied | 19 | 4 | | |
| Very dissatisfied | 10 | 1 | | |
| Not applicable | 20 | 2 | | |

Notes:

[22] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[23] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Frequency of Experiencing Unexpected Bleeding

| | |
|---|---|
| End point title | User Satisfaction – Frequency of Experiencing Unexpected Bleeding |
| End point description: | |
| The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase. | |
| End point type | Secondary |
| End point timeframe: | |
| At 18 months/EOS | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-----------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 ^[24] | 250 ^[25] | | |
| Units: subjects | | | | |
| Never | 145 | 219 | | |
| Seldom | 92 | 25 | | |
| Often | 17 | 5 | | |
| Very Often | 9 | 1 | | |

Notes:

[24] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[25] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Satisfaction With Menstrual Bleeding Absence

| | |
|-----------------|--|
| End point title | User Satisfaction – Satisfaction With Menstrual Bleeding Absence |
|-----------------|--|

End point description:

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 130 ^[26] | 14 ^[27] | | |
| Units: subjects | | | | |
| Very satisfied | 96 | 6 | | |
| Somewhat satisfied | 18 | 0 | | |
| Neither satisfied nor dissatisfied | 14 | 8 | | |
| Dissatisfied | 1 | 0 | | |
| Very dissatisfied | 1 | 0 | | |

Notes:

[26] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

[27] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Comparison of Menstrual Pain Intensity Between Now and Before Treatment

| | |
|-----------------|---|
| End point title | User Satisfaction – Comparison of Menstrual Pain Intensity Between Now and Before Treatment |
|-----------------|---|

End point description:

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-----------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 259 ^[28] | 247 ^[29] | | |
| Units: subjects | | | | |
| Decreased | 118 | 61 | | |
| Not changed | 102 | 169 | | |
| Increased | 39 | 17 | | |

Notes:

[28] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

[29] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Rating of Usual Menstrual Pain Intensity

| | |
|-----------------|--|
| End point title | User Satisfaction – Rating of Usual Menstrual Pain Intensity |
|-----------------|--|

End point description:

The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 18 months/EOS

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-----------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 261 ^[30] | 249 ^[31] | | |
| Units: subjects | | | | |
| None | 124 | 82 | | |
| Mild | 78 | 92 | | |
| Moderate | 43 | 67 | | |
| Severe | 16 | 8 | | |

Notes:

[30] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[31] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at Screening - Composite Score

| | |
|-----------------|--|
| End point title | EVAPIL-R Scores at Screening - Composite Score |
|-----------------|--|

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At screening

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 273 ^[32] | 275 ^[33] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | 0.9386 (± 0.8036) | 0.8846 (± 0.8231) | | |

Notes:

[32] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

[33] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at Screening - Bother Score

| | |
|---|---|
| End point title | EVAPIL-R Scores at Screening - Bother Score |
| End point description: | |
| The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item-specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. | |
| End point type | Secondary |
| End point timeframe: | |
| At screening | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 273 ^[34] | 276 ^[35] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | 0.5569 (± 0.4451) | 0.5188 (± 0.4406) | | |

Notes:

[34] - FAS (subjects with an assessment of the EVAPIL questionnaire where bother score could be calculated)

[35] - FAS (subjects with an assessment of the EVAPIL questionnaire where bother score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 6 Months

| | |
|-----------------|-----------------------------|
| End point title | EVAPIL-R Scores at 6 Months |
|-----------------|-----------------------------|

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item-specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 6 months

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 252 ^[36] | 243 ^[37] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Composite score | 1.3187 (± 0.9888) | 1.1537 (± 0.9947) | | |
| Bother score | 0.7364 (± 0.494) | 0.655 (± 0.5148) | | |

Notes:

[36] - FAS (subjects with an assessment of the EVAPIL questionnaire where the scores could be calculated)

[37] - FAS (subjects with an assessment of the EVAPIL questionnaire where the scores could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 12 Months - Composite Score

| | |
|-----------------|--|
| End point title | EVAPIL-R Scores at 12 Months - Composite Score |
|-----------------|--|

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item-specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 12 months where the composite score could be calculated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 12 months

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 229 ^[38] | 218 ^[39] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | 1.4022 (± 1.0126) | 1.0535 (± 0.8698) | | |

Notes:

[38] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

[39] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 12 Months - Bother Score

| | |
|-----------------|---|
| End point title | EVAPIL-R Scores at 12 Months - Bother Score |
|-----------------|---|

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item-specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 12 months where the bother score could be calculated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 12 months

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 233 ^[40] | 218 ^[41] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | 0.7789 (± 0.512) | 0.6015 (± 0.4663) | | |

Notes:

[40] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

[41] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 18 Months/EOS

| | |
|-----------------|----------------------------------|
| End point title | EVAPIL-R Scores at 18 Months/EOS |
|-----------------|----------------------------------|

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0),

frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item-specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 18 months/EOS where the scores could be calculated. The 18-month Treatment Visit served as the End-of-Study (EOS) Visit for participant in the COC group and LCS12 participant who did not enter the Extension Phase.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At 18 months/EOS | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|--------------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 260 ^[42] | 250 ^[43] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Composite score | 1.4804 (± 1.1926) | 1.0246 (± 0.9546) | | |
| Bother score | 0.8113 (± 0.5765) | 0.5908 (± 0.4836) | | |

Notes:

[42] - FAS (subjects with an assessment of the EVAPIL questionnaire where the scores could be calculated)

[43] - FAS (subjects with an assessment of the EVAPIL questionnaire where the scores could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Drop-out Rate

| | |
|---|--------------------------|
| End point title | Cumulative Drop-out Rate |
| End point description: | |
| The drop-out rate was the amount of subjects that could not complete the study for various reasons. Overall discontinuation rates were analyzed by Kaplan-Meier analyses and presented as cumulative half-yearly drop-out rates. '99999' indicates that the data were not applicable for that specific reporting group. Extension phase was only for LCS12 group. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 6, 12, 18, 24 and 36 months | |

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|-------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 279 ^[44] | 281 ^[45] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Up to 6 months | 7.53 | 11.39 | | |

| | | | | |
|-----------------|-------|-------|--|--|
| Up to 12 months | 13.26 | 21.71 | | |
| Up to 18 months | 18.64 | 27.4 | | |
| Up to 24 months | 30.85 | 99999 | | |
| Up to 36 months | 33.34 | 99999 | | |

Notes:

[44] - FAS

[45] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Pearl Index (PI)

| | |
|-----------------|------------------|
| End point title | Pearl Index (PI) |
|-----------------|------------------|

End point description:

The Pearl Index was defined as the number of pregnancies per 100 woman years (WYs). Given the assumption that the number of pregnancies follows a Poisson distribution, the Pearl Index thus is the mean of this distribution. '99999' indicates that the data were not applicable for that specific reporting group. Extension phase was only for LCS12 group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 18, 24, 36 months

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|---|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 279 ^[46] | 281 ^[47] | | |
| Units: pregnancies per 100 women years | | | | |
| arithmetic mean (confidence interval 95%) | | | | |
| Pearl index up to 18 months | 0.57 (0.07 to 2.05) | 1.82 (0.67 to 3.97) | | |
| Pearl index up to 24 months | 0.67 (0.14 to 1.95) | 99999 (99999 to 99999) | | |
| Pearl index up to 36 months | 0.65 (0.18 to 1.67) | 99999 (99999 to 99999) | | |

Notes:

[46] - FAS

[47] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Compliance Rate for Yasmin Pill Intake

| | |
|-----------------|--|
| End point title | Compliance Rate for Yasmin Pill Intake |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 18 months

| | | | | |
|-------------------------------|--------------------------------------|--|--|--|
| End point values | EE30/DRSP (Yasmin, BAY86-5131) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 281 ^[48] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Missing | 2.8 | | | |
| Compliance ≤75% | 2.1 | | | |
| Compliance >75% | 95 | | | |

Notes:

[48] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study Treatment

| | |
|-----------------|--|
| End point title | User Satisfaction – Acceptability of the Administration of Study Treatment |
|-----------------|--|

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without I/D, acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 6 months

| | | | | |
|----------------------------------|-----------------------------------|--------------------------------------|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 256 ^[49] | 244 ^[50] | | |
| Units: subjects | | | | |
| Acceptable without I/D | 163 | 192 | | |
| Acceptable with some I/D | 87 | 48 | | |
| Not acceptable with moderate I/D | 4 | 4 | | |
| Not acceptable with extreme I/D | 2 | 0 | | |

Notes:

[49] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[50] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study Treatment

| | |
|-----------------|--|
| End point title | User Satisfaction – Acceptability of the Administration of Study Treatment |
|-----------------|--|

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without I/D, acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At 12 months

| End point values | LCS12 (Jaydess, BAY86-5028) | EE30/DRSP (Yasmin, BAY86-5131) | | |
|----------------------------------|-----------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 237 ^[51] | 220 ^[52] | | |
| Units: subjects | | | | |
| Acceptable without I/D | 152 | 185 | | |
| Acceptable with some I/D | 74 | 33 | | |
| Not acceptable with moderate I/D | 9 | 2 | | |
| Not acceptable with extreme I/D | 1 | 0 | | |

Notes:

[51] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[52] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cumulative Number of Subjects With Partial or Total Expulsion

| | |
|-----------------|---|
| End point title | Cumulative Number of Subjects With Partial or Total Expulsion |
|-----------------|---|

End point description:

Total expulsion is confirmed if the IUS is observed in the vagina, the IUS is not shown in the uterine cavity by ultrasound, and / or the subject confirms that the system was expelled. Partial expulsion is diagnosed if the IUS can be partially seen in the vagina or is displaced in the cervical canal.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 18, 24, 36 months

| | | | | |
|-----------------------------------|-----------------------------------|--|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 279 ^[53] | | | |
| Units: subjects | | | | |
| Partial expulsion up to 18 months | 0 | | | |
| Total expulsion up to 18 months | 0 | | | |
| Partial expulsion up to 24 months | 1 | | | |
| Total expulsion up to 24 months | 0 | | | |
| Partial expulsion up to 36 months | 1 | | | |
| Total expulsion up to 36 months | 0 | | | |

Notes:

[53] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Investigator's Evaluation of Successful IUS Insertion Procedure

| | |
|-----------------|---|
| End point title | Investigator's Evaluation of Successful IUS Insertion Procedure |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 18 months

| | | | | |
|-----------------------------|-----------------------------------|--|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 279 ^[54] | | | |
| Units: subjects | | | | |
| Easy | 247 | | | |
| Slightly difficult | 31 | | | |
| Very difficult | 1 | | | |

Notes:

[54] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' Evaluation of Pain During Successful IUS Insertion Procedure

| | |
|-----------------|--|
| End point title | Subjects' Evaluation of Pain During Successful IUS Insertion Procedure |
|-----------------|--|

End point description:

| | |
|----------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Up to 18 months | |

| | | | | |
|-----------------------------|-----------------------------------|--|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 279 ^[55] | | | |
| Units: subjects | | | | |
| None | 49 | | | |
| Mild | 125 | | | |
| Moderate | 80 | | | |
| Severe | 25 | | | |

Notes:

[55] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Investigator's Evaluation of IUS Removal Procedure

| | |
|-----------------|--|
| End point title | Investigator's Evaluation of IUS Removal Procedure |
|-----------------|--|

End point description:

| | |
|----------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Up to 36 months | |

| | | | | |
|-----------------------------|-----------------------------------|--|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 267 ^[56] | | | |
| Units: subjects | | | | |
| Easy | 252 | | | |
| Slightly difficult | 11 | | | |
| Very difficult | 4 | | | |

Notes:

[56] - FAS (only subjects in the LCS12 arm with documented removal of the IUS)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' Evaluation of Pain During IUS Removal Procedure

| | |
|------------------------|---|
| End point title | Subjects' Evaluation of Pain During IUS Removal Procedure |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| Up to 36 months | |

| | | | | |
|-----------------------------|-----------------------------------|--|--|--|
| End point values | LCS12 (Jaydess, BAY86-5028) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 267 ^[57] | | | |
| Units: subjects | | | | |
| None | 136 | | | |
| Mild | 96 | | | |
| Moderate | 30 | | | |
| Severe | 5 | | | |

Notes:

[57] - FAS (only subjects in the LCS12 arm with documented removal of the IUS)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment until 36 months/EOS visit.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | EE30/DRSP (Yasmin, BAY86-5131) |
|-----------------------|--------------------------------|

Reporting group description:

Participants received combined oral contraceptive (COC) tablet Yasmin containing 30 micron ethinyl estradiol (EE) and 3 mg drospirenone (DRSP) for 18 months/19 cycles.

| | |
|-----------------------|---------------------------|
| Reporting group title | LCS12 (Skyla, BAY86-5028) |
|-----------------------|---------------------------|

Reporting group description:

Participants received LCS12 (low dose levonorgestrel [LNG] intrauterine delivery system [IUS]) with an initial in vitro release rate of 12 micron LNG per day for 18 months with optional extension to 36 months.

| Serious adverse events | EE30/DRSP (Yasmin, BAY86-5131) | LCS12 (Skyla, BAY86-5028) | |
|---|--------------------------------|---------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 281 (1.78%) | 22 / 279 (7.89%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Borderline ovarian tumour | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervix carcinoma stage 0 | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|--|
| Laceration | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 0 / 279 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 2 / 279 (0.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle injury | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 0 / 279 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Breast prosthesis implantation | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mammoplasty | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myomectomy | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 0 / 279 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral hernia | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Breast fibrosis | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Basedow's disease | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Exostosis | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nose deformity | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 2 / 281 (0.71%) | 1 / 279 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 0 / 279 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| | | | |
|---|--------------------------------|---------------------------|--|
| Non-serious adverse events | EE30/DRSP (Yasmin, BAY86-5131) | LCS12 (Skyla, BAY86-5028) | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 148 / 281 (52.67%) | 215 / 279 (77.06%) | |
| Surgical and medical procedures | | | |
| Wisdom teeth removal | | | |

| | | | |
|--|------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 281 (0.36%) 1 | 5 / 279 (1.79%) 5 | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 2 / 281 (0.71%) 2 | 3 / 279 (1.08%) 3 | |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 1 / 281 (0.36%) 1 | 3 / 279 (1.08%) 3 | |
| Breast tenderness subjects affected / exposed occurrences (all) | 2 / 281 (0.71%) 2 | 3 / 279 (1.08%) 3 | |
| Cervical dysplasia subjects affected / exposed occurrences (all) | 16 / 281 (5.69%) 17 | 35 / 279 (12.54%) 44 | |
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 26 / 281 (9.25%) 73 | 47 / 279 (16.85%) 76 | |
| Dyspareunia subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 4 / 279 (1.43%) 4 | |
| Menorrhagia subjects affected / exposed occurrences (all) | 5 / 281 (1.78%) 5 | 6 / 279 (2.15%) 6 | |
| Metrorrhagia subjects affected / exposed occurrences (all) | 1 / 281 (0.36%) 1 | 10 / 279 (3.58%) 14 | |
| Ovarian cyst subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 18 / 279 (6.45%) 22 | |
| Ovarian cyst ruptured subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 4 / 279 (1.43%) 4 | |
| Pelvic pain | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 281 (0.00%) | 13 / 279 (4.66%) | |
| occurrences (all) | 0 | 15 | |
| Vaginal discharge | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 12 / 279 (4.30%) | |
| occurrences (all) | 0 | 12 | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 8 / 279 (2.87%) | |
| occurrences (all) | 0 | 8 | |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 3 / 279 (1.08%) | |
| occurrences (all) | 2 | 3 | |
| Genital haemorrhage | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 6 / 279 (2.15%) | |
| occurrences (all) | 0 | 8 | |
| Coital bleeding | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 5 / 279 (1.79%) | |
| occurrences (all) | 1 | 5 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 281 (1.07%) | 2 / 279 (0.72%) | |
| occurrences (all) | 3 | 2 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 281 (0.71%) | 7 / 279 (2.51%) | |
| occurrences (all) | 2 | 8 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 2 / 279 (0.72%) | |
| occurrences (all) | 4 | 2 | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 0 / 279 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Irritability | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 3 / 279 (1.08%) | |
| occurrences (all) | 1 | 3 | |
| Libido decreased | | | |

| | | | |
|---|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 3 / 279 (1.08%) 3 | |
| Mood altered subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 1 / 279 (0.36%) 1 | |
| Investigations | | | |
| Smear cervix abnormal subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 5 / 279 (1.79%) 5 | |
| Weight decreased subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 3 / 279 (1.08%) 3 | |
| Weight increased subjects affected / exposed occurrences (all) | 8 / 281 (2.85%) 8 | 10 / 279 (3.58%) 10 | |
| Human papilloma virus test positive subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 5 / 279 (1.79%) 6 | |
| Chlamydia test positive subjects affected / exposed occurrences (all) | 2 / 281 (0.71%) 2 | 4 / 279 (1.43%) 4 | |
| Injury, poisoning and procedural complications | | | |
| Joint dislocation subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 4 / 279 (1.43%) 5 | |
| Contusion subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 0 / 279 (0.00%) 0 | |
| Procedural pain subjects affected / exposed occurrences (all) | 1 / 281 (0.36%) 2 | 10 / 279 (3.58%) 11 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 32 / 281 (11.39%) 54 | 26 / 279 (9.32%) 93 | |
| Migraine | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 5 / 281 (1.78%) 11 | 2 / 279 (0.72%) 2 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed occurrences (all) | 0 / 281 (0.00%) 0 | 3 / 279 (1.08%) 3 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed occurrences (all) | 4 / 281 (1.42%) 5 | 21 / 279 (7.53%) 31 | |
| Abdominal pain lower | | | |
| subjects affected / exposed occurrences (all) | 5 / 281 (1.78%) 5 | 12 / 279 (4.30%) 22 | |
| Abdominal pain upper | | | |
| subjects affected / exposed occurrences (all) | 6 / 281 (2.14%) 6 | 3 / 279 (1.08%) 4 | |
| Constipation | | | |
| subjects affected / exposed occurrences (all) | 4 / 281 (1.42%) 4 | 0 / 279 (0.00%) 0 | |
| Diarrhoea | | | |
| subjects affected / exposed occurrences (all) | 9 / 281 (3.20%) 11 | 1 / 279 (0.36%) 2 | |
| Gastritis | | | |
| subjects affected / exposed occurrences (all) | 4 / 281 (1.42%) 5 | 5 / 279 (1.79%) 5 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed occurrences (all) | 3 / 281 (1.07%) 3 | 5 / 279 (1.79%) 5 | |
| Nausea | | | |
| subjects affected / exposed occurrences (all) | 14 / 281 (4.98%) 16 | 9 / 279 (3.23%) 21 | |
| Toothache | | | |
| subjects affected / exposed occurrences (all) | 2 / 281 (0.71%) 2 | 4 / 279 (1.43%) 5 | |
| Vomiting | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 8 / 281 (2.85%) 9 | 4 / 279 (1.43%) 4 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 6 / 281 (2.14%) | 34 / 279 (12.19%) | |
| occurrences (all) | 6 | 41 | |
| Rash | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences (all) | 0 | 3 | |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences (all) | 0 | 3 | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 2 / 281 (0.71%) | 3 / 279 (1.08%) | |
| occurrences (all) | 2 | 3 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 8 / 279 (2.87%) | |
| occurrences (all) | 6 | 8 | |
| Infections and infestations | | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 6 / 281 (2.14%) | 5 / 279 (1.79%) | |
| occurrences (all) | 6 | 5 | |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 3 / 281 (1.07%) | 18 / 279 (6.45%) | |
| occurrences (all) | 3 | 21 | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 5 / 279 (1.79%) | |
| occurrences (all) | 6 | 5 | |
| Cystitis | | | |
| subjects affected / exposed | 15 / 281 (5.34%) | 23 / 279 (8.24%) | |
| occurrences (all) | 19 | 31 | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences (all) | 0 | 3 | |

| | | |
|-----------------------------|------------------|------------------|
| Gastroenteritis | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 5 / 279 (1.79%) |
| occurrences (all) | 4 | 5 |
| Gonorrhoea | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) |
| occurrences (all) | 0 | 3 |
| Influenza | | |
| subjects affected / exposed | 3 / 281 (1.07%) | 5 / 279 (1.79%) |
| occurrences (all) | 3 | 9 |
| Nasopharyngitis | | |
| subjects affected / exposed | 13 / 281 (4.63%) | 22 / 279 (7.89%) |
| occurrences (all) | 17 | 43 |
| Sinusitis | | |
| subjects affected / exposed | 6 / 281 (2.14%) | 3 / 279 (1.08%) |
| occurrences (all) | 7 | 3 |
| Tonsillitis | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 7 / 279 (2.51%) |
| occurrences (all) | 5 | 7 |
| Urinary tract infection | | |
| subjects affected / exposed | 4 / 281 (1.42%) | 14 / 279 (5.02%) |
| occurrences (all) | 4 | 17 |
| Vaginal infection | | |
| subjects affected / exposed | 7 / 281 (2.49%) | 11 / 279 (3.94%) |
| occurrences (all) | 8 | 15 |
| Vaginitis gardnerella | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 4 / 279 (1.43%) |
| occurrences (all) | 1 | 6 |
| Vulvitis | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) |
| occurrences (all) | 0 | 3 |
| Vulvovaginal candidiasis | | |
| subjects affected / exposed | 6 / 281 (2.14%) | 15 / 279 (5.38%) |
| occurrences (all) | 7 | 19 |
| Vulvovaginitis | | |
| subjects affected / exposed | 3 / 281 (1.07%) | 4 / 279 (1.43%) |
| occurrences (all) | 5 | 5 |

| | | | |
|--------------------------------|-----------------|------------------|--|
| Tooth infection | | | |
| subjects affected / exposed | 3 / 281 (1.07%) | 0 / 279 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Chlamydial infection | | | |
| subjects affected / exposed | 1 / 281 (0.36%) | 3 / 279 (1.08%) | |
| occurrences (all) | 1 | 3 | |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 7 / 281 (2.49%) | 10 / 279 (3.58%) | |
| occurrences (all) | 7 | 13 | |
| Vulvovaginitis streptococcal | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences (all) | 0 | 3 | |
| Vaginitis chlamydial | | | |
| subjects affected / exposed | 0 / 281 (0.00%) | 3 / 279 (1.08%) | |
| occurrences (all) | 0 | 3 | |
| Candida infection | | | |
| subjects affected / exposed | 2 / 281 (0.71%) | 4 / 279 (1.43%) | |
| occurrences (all) | 2 | 4 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 15 March 2011 | The extension phase for LCS12 users was added. Several of the original exclusion criteria were clarified under Amendment 1. An 18-month Extension Phase for subjects in the LCS12 treatment group was added. The timing of Visit 2 and switching of subjects from other forms of contraception was modified. Modified the protocol in response to requests from German Health Authority, to state that in Germany, only a gynaecologist may (1) insert the LCS12 and (2) perform gynaecologic investigations and procedures required by the study protocol. The section on withdrawal of subjects from the study was modified to state that subjects experiencing new-onset of migraine with neurological symptoms, thromboembolic diseases during study treatment, icterus or pronounced increase in blood pressured MUST be withdrawn from treatment. The size of ovarian cysts to be reported as AEs from 5 cm to >3 cm was changed. Discontinued collection of dysmenorrhea data in the subjects' diaries. |
| 22 July 2011 | The primary endpoint was clarified. Instructions regarding the use of backup contraception by LCS12 subjects who prematurely discontinued the study were modified. Safety follow-up and EOS assessments for subjects who prematurely discontinued the study was clarified. Clarified protocol to ensure that all pregnancies occurring during the study were appropriately reported to the Sponsor, not only those occurring while study drug was being used. Modified the protocol to indicate that the final clinical study report was not to include the results for the assessment of return to fertility as these data would not be available at the time of database closure. Corrected inconsistent information in the protocol regarding the time allowed between the Screening Visit and Treatment-assignment Visit. Changed definition of a compliant cycle in the COC group to indicate that no tablet could be forgotten on Cycle Days 1 through 21 and that the cycle length was to be no more than 28 days. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported