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	• 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	±		
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 appilcable 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 appilcable 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	1 / 281 (0.36%)	5 / 279 (1.79%)	
occurrences (all)	1	5	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 281 (0.71%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 281 (0.36%)	3 / 279 (1.08%)	
occurrences (all)	1	3	
Breast tenderness			
subjects affected / exposed	2 / 281 (0.71%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Cervical dysplasia			
subjects affected / exposed	16 / 281 (5.69%)	35 / 279 (12.54%)	
occurrences (all)	17	44	
Dysmenorrhoea			
subjects affected / exposed	26 / 281 (9.25%)	47 / 279 (16.85%)	
occurrences (all)	73	76	
Dyspareunia			
subjects affected / exposed	0 / 281 (0.00%)	4 / 279 (1.43%)	
occurrences (all)	0	4	
Menorrhagia			
subjects affected / exposed	5 / 281 (1.78%)	6 / 279 (2.15%)	
occurrences (all)	5	6	
Metrorrhagia			
subjects affected / exposed	1 / 281 (0.36%)	10 / 279 (3.58%)	
occurrences (all)	1	14	
Ovarian cyst			
subjects affected / exposed	0 / 281 (0.00%)	18 / 279 (6.45%)	
occurrences (all)	0	22	
Ovarian cyst ruptured			
subjects affected / exposed	0 / 281 (0.00%)	4 / 279 (1.43%)	
occurrences (all)	0	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	3 / 281 (1.07%)	3 / 279 (1.08%)	
occurrences (all)	3	3	
Mood altered			
subjects affected / exposed	3 / 281 (1.07%)	1 / 279 (0.36%)	
occurrences (all)	3	1	
Investigations			
Smear cervix abnormal			
subjects affected / exposed	0 / 281 (0.00%)	5 / 279 (1.79%)	
occurrences (all)	0	5	
Weight decreased			
subjects affected / exposed	3 / 281 (1.07%)	3 / 279 (1.08%)	
occurrences (all)	3	3	
Weight increased			
subjects affected / exposed	8 / 281 (2.85%)	10 / 279 (3.58%)	
occurrences (all)	8	10	
Human papilloma virus test positive			
subjects affected / exposed	3 / 281 (1.07%)	5 / 279 (1.79%)	
occurrences (all)	3	6	
Chlamydia test positive			
subjects affected / exposed	2 / 281 (0.71%)	4 / 279 (1.43%)	
occurrences (all)	2	4	
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 281 (0.00%)	4 / 279 (1.43%)	
occurrences (all)	0	5	
Contusion			
subjects affected / exposed	3 / 281 (1.07%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Procedural pain			
subjects affected / exposed	1 / 281 (0.36%)	10 / 279 (3.58%)	
occurrences (all)	2	11	
Nervous system disorders			
Headache			
subjects affected / exposed	32 / 281 (11.39%)	26 / 279 (9.32%)	
occurrences (all)	54	93	
Migraine			

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

subjects affected / exposed	8 / 281 (2.85%)	4 / 279 (1.43%)	
occurrences (all)	9	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