Clinical trial results:
Multi-center, randomized, comparator-controlled, single-blind, parallel-group study to investigate the pharmacodynamics, pharmacokinetics and safety of an intrauterine system releasing BAY 1007626, as compared with Mirena and Jaydess, in a combined proof-of-concept and dose-finding study in healthy pre-menopausal women treated for 90 days

Summary

EudraCT number	2013-003980-74
Trial protocol	DE GB NL
Global end of trial date	22 July 2016

Results information

Result version number	v1 (current)
This version publication date	07 June 2017
First version publication date	07 June 2017

Trial information

Trial identification

Sponsor protocol code	BAY1007626/15731

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02490774
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Bayer Clinical Trial Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Bayer Clinical Trial Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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	22 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 July 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate local and systemic effects of BAY1007626 on:
– Number of bleeding and spotting days,
– Endometrial histology,
– Ovulation (as surrogate for systemic effects).

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. Before entering the study, the informed consent form was read by and explained to all subjects. 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	22 June 2015
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	Netherlands: 59
Country: Number of subjects enrolled	United Kingdom: 32
Country: Number of subjects enrolled	Germany: 110
Worldwide total number of subjects	201
EEA total number of subjects	201

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)	201
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 9 study centers in multiple countries: Germany, the Netherlands and the United Kingdom between 22 June 2015 (first subject first visit) and 26 May 2016 (last subject last visit).

Pre-assignment

Screening details:

Overall, 395 subjects were screened, of these 194 subjects were screen failures. A total of 201 subjects were randomized: 19 subjects were never administered study drug and 182 subjects were treated and of them 126 completed the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	BAY1007626, 5 microgram (mcg)

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.

Arm type	Experimental
Investigational medicinal product name	BAY1007626
Investigational medicinal product code	BAY1007626
Other name	
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.

Arm title	BAY1007626, 15 mcg

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.

Arm type	Experimental
Investigational medicinal product name	BAY1007626
Investigational medicinal product code	BAY1007626
Other name	
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.

Arm title	BAY1007626, 30 mcg

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.

Arm type	Experimental

Investigational medicinal product name	BAY1007626
Investigational medicinal product code	BAY1007626
Other name	
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.

Arm title	BAY1007626, 60 mcg

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.

Arm type	Experimental
Investigational medicinal product name	BAY1007626
Investigational medicinal product code	BAY1007626
Other name	
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.

Arm title	Levonorgestrel (Jaydess, BAY86-5028)

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.

Arm type	Active comparator
Investigational medicinal product name	Levonorgestrel
Investigational medicinal product code	BAY86-5028
Other name	Jaydess
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.

Arm title	Levonorgestrel (Mirena, BAY86-5028)

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.

Arm type	Active comparator
Investigational medicinal product name	Levonorgestrel
Investigational medicinal product code	BAY86-5028
Other name	Mirena
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.

Number of subjects in period 1	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg
Started	39	36	37
Completed	22	24	26
Not completed	17	12	11
Protocol violation	2	1	1
Adverse event	4	-	1
Study terminated by sponsor	11	9	8
Withdrawal by subject	-	2	1

Number of subjects in period 1	BAY1007626, 60 mcg	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)
Started	39	12	38
Completed	24	10	24
Not completed	15	2	14
Protocol violation	2	1	1
Adverse event	3	-	3
Study terminated by sponsor	8	1	9
Withdrawal by subject	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	BAY1007626, 5 microgram (mcg)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 15 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 30 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 60 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.	
Reporting group title	Levonorgestrel (Jaydess, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.	
Reporting group title	Levonorgestrel (Mirena, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.	

Reporting group values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg
Number of subjects	39	36	37
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	29.9	27.8	30.7
standard deviation	± 6.2	± 5.4	± 5.1
Gender categorical			
Units: Subjects			
Female	39	36	37

Reporting group values	BAY1007626, 60 mcg	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)
Number of subjects	39	12	38
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	29.9	29.4	29.1

standard deviation	± 5.3	± 6	± 5.3

Gender categorical Units: Subjects			
Female	39	12	38

Reporting group values	Total		
Number of subjects	201		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	201		

End points

End points reporting groups

Reporting group title	BAY1007626, 5 microgram (mcg)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 15 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 30 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 60 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.	
Reporting group title	Levonorgestrel (Jaydess, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.	
Reporting group title	Levonorgestrel (Mirena, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SAF (N= 182) included all subjects who received study medication.	
Subject analysis set title	Pharmacodynamic analysis set 1 (PDS1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PDS1 (N= 134) included all subjects within the safety analysis set without major protocol deviations who were non completers with at least 60 days of treatment, and for whom not more than 9 entries in the bleeding diary were missing during the treatment period.	
Subject analysis set title	Pharmacodynamic analysis set 2 (PDS2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PDS2 (N= 44) included all subjects who received study medication, without major protocol violations for whom the pharmacodynamics biopsy was evaluated.	
Subject analysis set title	Pharmacodynamic analysis set 3 (PDS3)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PDS3 (N= 167) included all subjects from the safety analysis set without major protocol deviations who were treated for at least 40 days (a time span that would cover at least one menstrual cycle in an untreated woman), and for whom weekly measurements of progesterone were performed as outlined in the protocol.	

Primary: Number of Bleeding and Spotting Days During the 90 Days Treatment Period

End point title	Number of Bleeding and Spotting Days During the 90 Days Treatment Period

End point description:

The total number of bleeding and spotting days per subject under treatment were determined as the total number of days for which a code greater than (>) 1 had been observed. The following codes 1,2,3,4,5 were given for the below mentioned categories.
1) None: no bleeding
2) Spotting: less than associated with normal menstruation relative to the subject's experience, with no need for sanitary protection (except for panty liners)
3) Light: less than associated with normal menstruation relative to the subject's experience, with need for sanitary protection
4) Normal: like normal menstruation relative to the subject's experience
5) Heavy: more than normal menstruation relative to the subject's experience

End point type	Primary

End point timeframe:

Day 1 to Day 90

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[1]	17[2]	22[3]	20[4]
Units: days				
arithmetic mean (standard deviation)	38.0526 (± 18.0045)	36.2353 (± 16.1072)	49.8636 (± 15.3973)	42.35 (± 19.2826)

Notes:

[1] - PDS1 with number of subjects evaluable for this specific endpoint

[2] - PDS1 with number of subjects evaluable for this specific endpoint

[3] - PDS1 with number of subjects evaluable for this specific endpoint

[4] - PDS1 with number of subjects evaluable for this specific endpoint

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[5]	20[6]		
Units: days				
arithmetic mean (standard deviation)	40.1111 (± 15.8623)	37.3 (± 12.2178)		

Notes:

[5] - PDS1 with number of subjects evaluable for this specific endpoint

[6] - PDS1 with number of subjects evaluable for this specific endpoint

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 5 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95 percent (%) confidence interval (CI) estimates were given for the mean difference between Mirena and BAY1007626, 5 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

Comparison groups	Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 5

	microgram (mcg)
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	11.6

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 15 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 15 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

Comparison groups	Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 15 mcg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	9.5

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 30 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 30 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

Comparison groups	Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 30 mcg
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference
Point estimate	14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.9
upper limit	21.6

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 60 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 60 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

Comparison groups	Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 60 mcg
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	16.2

Primary: Number of Subjects With Endometrium Proliferative

End point title	Number of Subjects With Endometrium Proliferative[7]

End point description:

Endometrial histology was evaluated in endometrial biopsy specimen taken. The histology of the specimen was evaluated by blinded reading. As the study was terminated prematurely, biopsies were only assessed by blinded read assessment in a few subjects. Endometrial biopsies were taken between Days 41 and 90 during treatment and on Day 9 during follow-up. In the below table, "n" indicates the number of subjects analysed for the specified parameter at given time point for each arm, respectively.

End point type	Primary

End point timeframe:

Treatment (between Days 41 and 90), post-treatment, follow-up (Day 9 during follow-up)

Notes:

[7] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[8]	7[9]	11[10]	8[11]
Units: subjects				
Treatment (n= 4,7,11,8,7,6)	0	0	0	0
Post-treatment (n= 0,1,0,0,0,0)	0	0	0	0
Follow-up (n= 2,1,4,0,3,2)	2	1	4	0

Notes:

[8] - PDS2

[9] - PDS2

[10] - PDS2

[11] - PDS2

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[12]	6[13]		
Units: subjects				
Treatment (n= 4,7,11,8,7,6)	0	1		
Post-treatment (n= 0,1,0,0,0,0)	0	0		
Follow-up (n= 2,1,4,0,3,2)	3	1		

Notes:

[12] - PDS2

[13] - PDS2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Ovulation During Treatment

End point title	Number of Subjects With Ovulation During Treatment[14]

End point description:

Ovulation activity is defined as:
In the weekly visit group: frequency of ovulation (based on assessments of progesterone serum levels > 5 nanomoles/liter)
In the dense visit group: frequency of ovulation (based on evaluation of Hoogland score of 6).

End point type	Primary

End point timeframe:

Day 1 to Day 90

Notes:

[14] - 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: EudraCT database does not allow to report only one treatment group in statistical analyses section. Due to this format constraint, charts have been uploaded with the accurate details of statistical analyses for this endpoint. Please find the statistical analyses in the attachment below.

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31[15]	31[16]	31[17]	32[18]
Units: subjects	28	29	29	19

Notes:

[15] - PDS3

[16] - PDS3

[17] - PDS3

[18] - PDS3

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[19]	31[20]		
Units: subjects	10	19		

Notes:
[19] - PDS3
[20] - PDS3

Attachments (see zip file)	15731_Statistical Analysis_Primary OM/15731_Statistical

Statistical analyses

No statistical analyses for this end point

Secondary: Endometrial Thickness

End point title	Endometrial Thickness

End point description:

Endometrium is the tissue lining the inner cavity of the uterus. Endometrial thickness was measured by transvaginal ultrasound (TVU). TUV examination was performed by a trained qualified member of the investigation team. The endometrial thickness was measured in the medio-sagittal section as double layer in millimetres. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore, endometrial thickness was not measured.

End point type	Secondary

End point timeframe:

From start of treatment until end of study

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[21]	0[22]	0[23]	0[24]
Units: subjects				

Notes:
[21] - As the primary endpoints could not be met, the study was discontinued permanently.
[22] - As the primary endpoints could not be met, the study was discontinued permanently.
[23] - As the primary endpoints could not be met, the study was discontinued permanently.
[24] - As the primary endpoints could not be met, the study was discontinued permanently.

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	0[26]		
Units: subjects				

Notes:
[25] - As the primary endpoints could not be met, the study was discontinued permanently.
[26] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding Characterization (Intensity and Pattern)

End point title	Bleeding Characterization (Intensity and Pattern)

End point description:

A bleeding/spotting episode is defined as day(s) with bleeding/spotting preceded and followed by at least 2 bleed-free days.
For bleeding pattern the following dichotomous variables were analysed:
a) Irregular bleeding: 3 to 5 bleeding/spotting episodes and less than 3 bleeding/spotting-free intervals of 14 or more days.
b) Prolonged bleeding: any bleeding/spotting episode lasting more than 14 days.
c) Frequent bleeding: more than 5 bleeding/spotting episodes.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[27]	17[28]	22[29]	20[30]
Units: subjects				
Irregular bleeding	8	8	12	13
Prolonged bleeding	9	7	14	13
Frequent bleeding	4	6	3	2

Notes:

[27] - PDS with number of subjects evaluable for this specific endpoint

[28] - PDS with number of subjects evaluable for this specific endpoint

[29] - PDS with number of subjects evaluable for this specific endpoint

[30] - PDS

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[31]	20[32]		
Units: subjects				
Irregular bleeding	7	11		
Prolonged bleeding	4	11		
Frequent bleeding	0	5		

Notes:

[31] - PDS

[32] - PDS with number of subjects evaluable for this specific endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Levels of Hormones (Estradiol, Progesterone, Luteinizing Hormone, Follicle-Stimulating Hormone)

End point title	Serum Levels of Hormones (Estradiol, Progesterone, Luteinizing Hormone, Follicle-Stimulating Hormone)

End point description:

Blood samples for the determination of estradiol, progesterone, luteinizing hormone, follicle-stimulating

hormone levels in serum were taken during the treatment period and the follow-up period. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore serum levels of hormones in blood were not evaluated.

End point type	Secondary

End point timeframe:

From start of treatment until end of study

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[33]	0[34]	0[35]	0[36]
Units: subjects				

Notes:

[33] - As the primary endpoints could not be met, the study was discontinued permanently.

[34] - As the primary endpoints could not be met, the study was discontinued permanently.

[35] - As the primary endpoints could not be met, the study was discontinued permanently.

[36] - As the primary endpoints could not be met, the study was discontinued permanently.

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[37]	0[38]		
Units: subjects				

Notes:

[37] - As the primary endpoints could not be met, the study was discontinued permanently.

[38] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly and another medical important serious event as judged by investigator. AE/SAEs that started or worsened after study drug treatment were recorded as TEAE/TESAEs.

End point type	Secondary

End point timeframe:

From start of study treatment until end of study

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[39]	33[40]	33[41]	34[42]
Units: subjects				
TEAEs	32	28	28	32
TESAEs	2	0	0	0

Notes:

[39] - SAF

[40] - SAF

[41] - SAF

[42] - SAF

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[43]	35[44]		
Units: subjects				
TEAEs	11	33		
TESAEs	0	0		

Notes:

[43] - SAF

[44] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Drug Concentration of BAY1007626 After Insertion of Intrauterine System (Cmax) in Plasma

End point title	Maximum Observed Drug Concentration of BAY1007626 After Insertion of Intrauterine System (Cmax) in Plasma

End point description:

Maximum observed drug concentration of BAY1007626 after insertion of intrauterine system in plasma. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

End point type	Secondary

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[45]	0[46]	0[47]	0[48]
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[45] - As the primary endpoints could not be met, the study was discontinued permanently.

[46] - As the primary endpoints could not be met, the study was discontinued permanently.

[47] - As the primary endpoints could not be met, the study was discontinued permanently.

[48] - As the primary endpoints could not be met, the study was discontinued permanently.

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[49]	0[50]		
Units: microgram per liter (mcg/L)				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[49] - As the primary endpoints could not be met, the study was discontinued permanently.

[50] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Versus Time Curve (AUC) of BAY1007626 in Plasma After Insertion of Intrauterine System

End point title	Area Under the Concentration Versus Time Curve (AUC) of BAY1007626 in Plasma After Insertion of Intrauterine System

End point description:

Area under the concentration versus time curve of BAY1007626 in plasma after insertion of intrauterine system. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

End point type	Secondary

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[51]	0[52]	0[53]	0[54]
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[51] - As the primary endpoints could not be met, the study was discontinued permanently.

[52] - As the primary endpoints could not be met, the study was discontinued permanently.

[53] - As the primary endpoints could not be met, the study was discontinued permanently.

[54] - As the primary endpoints could not be met, the study was discontinued permanently.

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[55]	0[56]		
Units: microgram*hour per liter (mcg*h/L)				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[55] - As the primary endpoints could not be met, the study was discontinued permanently.

[56] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life Associated With the Terminal Slope (t1/2) of BAY1007626 in Plasma

End point title	Half-life Associated With the Terminal Slope (t1/2) of BAY1007626 in Plasma

End point description:

Half-life associated with the terminal slope of BAY1007626 in plasma. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

End point type	Secondary

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

End point values	BAY1007626, 5 microgram (mcg)	BAY1007626, 15 mcg	BAY1007626, 30 mcg	BAY1007626, 60 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[57]	0[58]	0[59]	0[60]
Units: hours				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[57] - As the primary endpoints could not be met, the study was discontinued permanently.

[58] - As the primary endpoints could not be met, the study was discontinued permanently.

[59] - As the primary endpoints could not be met, the study was discontinued permanently.

[60] - As the primary endpoints could not be met, the study was discontinued permanently.

End point values	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[61]	0[62]		
Units: hours				
geometric mean (geometric coefficient of variation)	()	()		

Notes:

[61] - As the primary endpoints could not be met, the study was discontinued permanently.

[62] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study treatment until end of study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	BAY1007626, 5 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 15 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 30 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.	
Reporting group title	BAY1007626, 60 mcg
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.	
Reporting group title	Levonorgestrel (Jaydess, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.	
Reporting group title	Levonorgestrel (Mirena, BAY86-5028)
Reporting group description:	
Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.	

Serious adverse events	BAY1007626, 5 mcg	BAY1007626, 15 mcg	BAY1007626, 30 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 33 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BAY1007626, 60 mcg	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	BAY1007626, 5 mcg	BAY1007626, 15 mcg	BAY1007626, 30 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 36 (88.89%)	28 / 33 (84.85%)	28 / 33 (84.85%)
Surgical and medical procedures			
Mole excision			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Dental care			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	1	1	1
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 36 (8.33%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	3	1	1
Feeling hot			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Hangover			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Social circumstances			
Tattoo			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast			

disorders			
Breast enlargement			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Breast pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	4	0	1
Breast tenderness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	7 / 36 (19.44%)	3 / 33 (9.09%)	1 / 33 (3.03%)
occurrences (all)	11	3	2
Dyspareunia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Galactorrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Menorrhagia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Nipple pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	6 / 33 (18.18%)
occurrences (all)	3	2	8
Ovulation pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Pelvic pain			

subjects affected / exposed	4 / 36 (11.11%)	1 / 33 (3.03%)	3 / 33 (9.09%)
occurrences (all)	13	2	3
Uterine polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge			
subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Vaginal odour			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	1	1	1
Uterine cyst			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Breast discomfort			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	3 / 33 (9.09%)
occurrences (all)	0	1	4
Vulvovaginal pruritus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 36 (2.78%)	4 / 33 (12.12%)	2 / 33 (6.06%)
occurrences (all)	1	5	2
Vulvovaginal burning sensation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal erythema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Dysphonia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Libido decreased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Listless			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Mood altered			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Mood swings			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0

Sleep disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Suicidal ideation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Affect lability			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device expulsion			
subjects affected / exposed	3 / 36 (8.33%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	3	0	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	2 / 33 (6.06%)
occurrences (all)	1	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	3 / 33 (9.09%)
occurrences (all)	1	2	3
Blood bilirubin increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Blood prolactin increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	3 / 36 (8.33%)	4 / 33 (12.12%)	2 / 33 (6.06%)
occurrences (all)	4	4	2
Haemoglobin decreased			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Monocyte count increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Red blood cell count decreased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Serum ferritin decreased			
subjects affected / exposed	2 / 36 (5.56%)	3 / 33 (9.09%)	0 / 33 (0.00%)
occurrences (all)	2	3	0
White blood cell count decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	2 / 36 (5.56%)	1 / 33 (3.03%)	2 / 33 (6.06%)
occurrences (all)	2	1	2
Urine bilirubin increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Nitrite urine present			

subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Protein urine present			
subjects affected / exposed	2 / 36 (5.56%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	2	1	1
Lymph node palpable			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Waist circumference increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Bilirubin urine present			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Traumatic haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Limb injury			

subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	4 / 36 (11.11%)	5 / 33 (15.15%)	5 / 33 (15.15%)
occurrences (all)	4	7	5
Ligament rupture			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Procedural nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	4 / 33 (12.12%)	1 / 33 (3.03%)
occurrences (all)	0	4	1
Headache			
subjects affected / exposed	14 / 36 (38.89%)	14 / 33 (42.42%)	14 / 33 (42.42%)
occurrences (all)	21	31	35
Hemiparesis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Muscle contractions involuntary			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Sinus headache			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Visual field defect			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Hemianaesthesia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Microcytic anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	3 / 36 (8.33%)	5 / 33 (15.15%)	5 / 33 (15.15%)
occurrences (all)	3	13	7
Abdominal pain lower			
subjects affected / exposed	8 / 36 (22.22%)	11 / 33 (33.33%)	11 / 33 (33.33%)
occurrences (all)	20	29	34
Abdominal pain upper			

subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Dental caries			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	3 / 33 (9.09%)
occurrences (all)	1	1	4
Dyspepsia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Gastrointestinal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 36 (11.11%)	2 / 33 (6.06%)	1 / 33 (3.03%)
occurrences (all)	4	2	1
Toothache			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	3 / 33 (9.09%)
occurrences (all)	2	0	3
Vomiting			
subjects affected / exposed	2 / 36 (5.56%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	3	1	1
Chapped lips			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 36 (8.33%)	1 / 33 (3.03%)	4 / 33 (12.12%)
occurrences (all)	3	2	4

Alopecia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Dry skin			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Hair texture abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Hirsutism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Psoriasis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Rash papular			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Skin discolouration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0

Skin disorder			
subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Skin irritation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
Dysuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
Ketonuria			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	1 / 33 (3.03%)
occurrences (all)	2	2	1
Pollakiuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Urobilinuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	3 / 36 (8.33%)	5 / 33 (15.15%)	0 / 33 (0.00%)
occurrences (all)	3	7	0
Joint swelling			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	2 / 33 (6.06%)
occurrences (all)	2	4	2
Myositis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Synovial cyst			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess oral			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Bacterial vaginosis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	3 / 33 (9.09%)
occurrences (all)	1	3	4
Diarrhoea infectious			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	3 / 36 (8.33%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	3	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
Gastrointestinal infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Gingivitis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	6 / 36 (16.67%)	6 / 33 (18.18%)	3 / 33 (9.09%)
occurrences (all)	8	8	3
Laryngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	14 / 36 (38.89%)	11 / 33 (33.33%)	13 / 33 (39.39%)
occurrences (all)	20	14	18
Otitis media			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Tooth infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Vaginitis bacterial			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	2 / 33 (6.06%)
occurrences (all)	4	0	2
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Food intolerance			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BAY1007626, 60 mcg	Levonorgestrel (Jaydess, BAY86-5028)	Levonorgestrel (Mirena, BAY86-5028)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 34 (94.12%)	11 / 11 (100.00%)	33 / 35 (94.29%)
Surgical and medical procedures			
Mole excision			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dental care			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Feeling hot			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hangover			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Tattoo			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			

Breast enlargement			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Breast pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Breast tenderness			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Dysmenorrhoea			
subjects affected / exposed	4 / 34 (11.76%)	2 / 11 (18.18%)	2 / 35 (5.71%)
occurrences (all)	6	2	2
Dyspareunia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Galactorrhoea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Metrorrhagia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nipple pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Ovarian cyst			
subjects affected / exposed	17 / 34 (50.00%)	2 / 11 (18.18%)	14 / 35 (40.00%)
occurrences (all)	24	2	21
Ovulation pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	1 / 34 (2.94%)	3 / 11 (27.27%)	4 / 35 (11.43%)
occurrences (all)	2	4	5

Uterine polyp			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	3 / 34 (8.82%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Vaginal odour			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Uterine cyst			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Breast discomfort			
subjects affected / exposed	4 / 34 (11.76%)	1 / 11 (9.09%)	3 / 35 (8.57%)
occurrences (all)	4	1	4
Vulvovaginal pruritus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal burning sensation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal erythema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 34 (0.00%)	2 / 11 (18.18%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Dysphonia			

subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	3
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Libido decreased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Listless			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	2
Mood swings			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1

Suicidal ideation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Affect lability			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Product issues			
Device expulsion			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	1
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)	2 / 11 (18.18%)	1 / 35 (2.86%)
occurrences (all)	1	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Blood prolactin increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	1 / 34 (2.94%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	3	3	1
Blood urine present			

subjects affected / exposed	3 / 34 (8.82%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	3	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Monocyte count increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	1 / 34 (2.94%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	3 / 35 (8.57%)
occurrences (all)	1	0	3
Urine bilirubin increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Nitrite urine present			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Platelet count increased			

subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Protein urine present			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Lymph node palpable			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Waist circumference increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Bilirubin urine present			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Ligament sprain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	3
Traumatic haematoma			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Procedural pain			

subjects affected / exposed	7 / 34 (20.59%)	2 / 11 (18.18%)	12 / 35 (34.29%)
occurrences (all)	10	2	13
Ligament rupture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 34 (2.94%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Headache			
subjects affected / exposed	15 / 34 (44.12%)	10 / 11 (90.91%)	11 / 35 (31.43%)
occurrences (all)	22	28	12
Hemiparesis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Syncope			

subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Visual field defect			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hemianaesthesia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Microcytic anaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	3 / 34 (8.82%)	1 / 11 (9.09%)	5 / 35 (14.29%)
occurrences (all)	4	1	6
Abdominal pain lower			
subjects affected / exposed	17 / 34 (50.00%)	7 / 11 (63.64%)	10 / 35 (28.57%)
occurrences (all)	38	18	17
Abdominal pain upper			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	0	1	2
Constipation			

subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 34 (5.88%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Flatulence			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 34 (8.82%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	3	1	2
Toothache			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Chapped lips			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 34 (5.88%)	1 / 11 (9.09%)	3 / 35 (8.57%)
occurrences (all)	2	1	4
Alopecia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Dry skin			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Hair texture abnormal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hirsutism			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Psoriasis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Rosacea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Skin irritation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	2 / 34 (5.88%)	1 / 11 (9.09%)	4 / 35 (11.43%)
occurrences (all)	4	2	6
Dysuria			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	2 / 34 (5.88%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	2	3	0
Ketonuria			
subjects affected / exposed	5 / 34 (14.71%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	5	1	3
Pollakiuria			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Renal pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Urobilinuria			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Leukocyturia			
subjects affected / exposed	4 / 34 (11.76%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	5	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	3 / 34 (8.82%)	2 / 11 (18.18%)	4 / 35 (11.43%)
occurrences (all)	3	2	4
Joint swelling			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 34 (2.94%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Myositis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 34 (2.94%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Synovial cyst			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abscess oral			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Bacterial vaginosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	2	0

Cystitis			
subjects affected / exposed	3 / 34 (8.82%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Diarrhoea infectious			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 34 (2.94%)	2 / 11 (18.18%)	0 / 35 (0.00%)
occurrences (all)	2	2	0

Laryngitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	13 / 34 (38.24%)	6 / 11 (54.55%)	13 / 35 (37.14%)
occurrences (all)	18	7	19
Otitis media			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	3 / 34 (8.82%)	1 / 11 (9.09%)	0 / 35 (0.00%)
occurrences (all)	3	1	0
Tooth infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Vaginitis bacterial			
subjects affected / exposed	1 / 34 (2.94%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 34 (0.00%)	1 / 11 (9.09%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Decreased appetite			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Food intolerance			
subjects affected / exposed	0 / 34 (0.00%)	0 / 11 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 May 2016	The underlying clinical development program had been discontinued permanently. An interim analysis had shown that one of the primary endpoints (reduction in number of bleeding and spotting days compared to Mirena during the first 90 days of treatment) could not be met. Without demonstrating superiority of this primary variable a further development of an IUS releasing BAY1007626 intended to reduce initial bleeding/ spotting after IUS insertion did not make sense and the development program was discontinued.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was discontinued permanently as the primary endpoints could not be met. Decimal places were automatically truncated if last decimal equals zero.

Notes: