



## Clinical trial results:

**A multi-center, double-blind, double-dummy, randomized, controlled, parallel-group study to assess efficacy and safety of SH T00658ID compared to SH D593B in the treatment of primary dysmenorrhea**

### Summary

EudraCT number	2008-005625-11
Trial protocol	DE IT
Global end of trial date	18 November 2010

### Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	26 June 2015

### Trial information

#### Trial identification

Sponsor protocol code	BAY86-5027/91781
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00909857
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Bayer HealthCare AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, 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	14 January 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 November 2010
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the study was to show superiority of SH T00658ID over SH D593B with respect to the number of days with dysmenorrheic pain (defined as pelvic pain during the menstrual/withdrawal bleeding episode and the 2 days before this episode) in a defined period, i.e. comparison between two treatment cycles and two baseline cycles.

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. Only after the subject voluntarily signed the informed consent form was he/she able to enter the study. If the subject was not capable of providing a signature, an oral statement of consent could have been given in the presence of a witness. Each subject was assured of the right to 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	15 April 2009
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	United States: 96
Country: Number of subjects enrolled	Italy: 59
Country: Number of subjects enrolled	Chile: 53
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Philippines: 97
Country: Number of subjects enrolled	Germany: 148
Worldwide total number of subjects	464
EEA total number of subjects	207

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	24
Adults (18-64 years)	440
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects aged 14 to 50 years with a need for oral contraception suffering from primary dysmenorrhea were recruited at specialized study sites.

### Pre-assignment

Screening details:

Out of 771 subjects screened, 264 failed screening, mostly due to not meeting in-/exclusion criteria (155), withdrawal of consent (49), loss to follow-up (36) or pregnancy (10). Thus, 507 subjects were randomized (253 to Estradiol valerate/Dienogest and 254 to Ethinyl estradiol/Levonorgestrel), out of which 464 subjects received treatment.

### Period 1

Period 1 title	Overall Study
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Carer, Subject, Investigator

Blinding implementation details:

For blinding purposes, a double-dummy design was used. The investigational and reference product were packed for a double-dummy design in one wallet with two blisters of 28 tablets each.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)

Arm description:

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.

Arm type	Experimental
Investigational medicinal product name	Placebo Match to SH T00658ID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.

Investigational medicinal product name	Estradiol Valerate, Dienogest (SH T00658ID)
Investigational medicinal product code	BAY86-5027
Other name	Natazia, Qlaira
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.

<b>Arm title</b>	Ethinyl Estradiol, Levonorgestrel (Miranova)
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Arm description:

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.

Arm type	Active comparator
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Investigational medicinal product name	Placebo Match to SH D593B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.

Investigational medicinal product name	Ethinyl Estradiol, Levonorgestrel (SH D593B)
Investigational medicinal product code	
Other name	Miranova
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.

Number of subjects in period 1	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)
Started	253	254
Treated	234	230
Completed	217	209
Not completed	36	45
Consent withdrawn by subject	6	10
Protocol violation	2	1
Pregnancy	1	-
Unknown	1	-
Adverse event	5	5
Lost to follow-up	2	5
Did not receive study medication	19	24

## Period 2

Period 2 title	Baseline period
Is this the baseline period?	Yes <sup>[1]</sup>
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Carer, Subject, Investigator

## Arms

Are arms mutually exclusive?	No
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<b>Arm title</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)
Arm description: Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.	
Arm type	Experimental
Investigational medicinal product name	Estradiol Valerate, Dienogest (SH T00658ID)
Investigational medicinal product code	BAY86-5027
Other name	Natazia, Qlaira
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.

Investigational medicinal product name	Placebo Match to SH T00658ID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.

<b>Arm title</b>	Ethinyl Estradiol, Levonorgestrel (Miranova)
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**Arm description:**

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.

Arm type	Active comparator
Investigational medicinal product name	Ethinyl Estradiol, Levonorgestrel (SH D593B)
Investigational medicinal product code	
Other name	Miranova
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.

Investigational medicinal product name	Placebo Match to SH D593B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

**Dosage and administration details:**

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.

**Notes:**

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

Justification: In overall trial, all subjects who were randomized were included and the baseline characteristics were provided only for subjects who were treated. Hence, the baseline period of treated subjects was created to publish the baseline characteristics data.

<b>Number of subjects in period 2</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)
Started	234	230
Completed	234	230

## Baseline characteristics

### Reporting groups

Reporting group title	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)
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Reporting group description:

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.

Reporting group title	Ethinyl Estradiol, Levonorgestrel (Miranova)
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Reporting group description:

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.

Reporting group values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)	Total
Number of subjects	234	230	464
Age categorical			
Units: Subjects			
less than 18 years of age	11	13	24
18 years of age or older	223	217	440
Age continuous			
Units: years			
arithmetic mean	28	27.6	
standard deviation	± 7.9	± 8	-
Gender categorical			
Units: Subjects			
Female	234	230	464



## End points

### End points reporting groups

Reporting group title	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)
Reporting group description: Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles.	
Reporting group title	Ethinyl Estradiol, Levonorgestrel (Miranova)
Reporting group description: Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles.	
Reporting group title	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)
Reporting group description: Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.	
Reporting group title	Ethinyl Estradiol, Levonorgestrel (Miranova)
Reporting group description: Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment 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: All subjects admitted to the treatment phase who took at least 1 tablet of study medication or comparator, and for whom at least 1 observation after admission to treatment was available were included in the FAS.	

### Primary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in the Number of Days With Dysmenorrheic Pain

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in the Number of Days With Dysmenorrheic Pain
End point description: Dysmenorrheic pain was defined as pelvic pain during the menstrual/withdrawal bleeding episode and the 2 days before this episode. Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).	
End point type	Primary
End point timeframe: Baseline period (2 baseline cycles, usually 56 days) versus (vs) treatment period (on-treatment cycles 2 and 3, usually 56 days)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[1]</sup>	219 <sup>[2]</sup>		
Units: days				
arithmetic mean (standard deviation)	-4.6 (± 4.6)	-4.2 (± 4.2)		

Notes:

[1] - FAS

[2] - FAS

## Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis 1
Statistical analysis description:	
An individual absolute change in days with dysmenorrheic pain from pretreatment was evaluated as number of days with dysmenorrheic pain during the treatment evaluation period minus number of days with dysmenorrheic pain during the pretreatment evaluation period.	
Comparison groups	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027) v Ethinyl Estradiol, Levonorgestrel (Miranova)
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3358
Method	t-test, 2-sided
Parameter estimate	Difference of mean changes from baseline
Point estimate	-0.404
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.227
upper limit	0.4196

## Secondary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in the Sum of Score Points of Dysmenorrheic Pain

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in the Sum of Score Points of Dysmenorrheic Pain
End point description:	
Dysmenorrheic pain: pelvic pain during menstrual/withdrawal bleeding (WB) episode and 2 days before. Scores per day: 0 No pain; 1 Mild pain with no need for painkiller; 2 Moderate pain with need for painkiller; 3 Severe pain with need for painkiller. Baseline period: 2 days before 1st menstrual bleeding until 3rd day before 3rd menstrual bleeding (normalized to standard 56-day period). Treatment period: 2 days before WB of 1st treatment cycle until 3rd day before WB of the cycle after 2nd treatment cycle (normalized to standard 56-day period). Score difference minimum -168 (best), maximum 168 (worst).	
End point type	Secondary
End point timeframe:	
Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[3]</sup>	219 <sup>[4]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	-10.6 (± 9.7)	-10 (± 8.9)		

Notes:

[3] - FAS

[4] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in Number of Days With Pelvic Pain Independent of Occurrence of Vaginal Bleeding

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in Number of Days With Pelvic Pain Independent of Occurrence of Vaginal Bleeding
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End point description:

Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).

End point type	Secondary
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End point timeframe:

Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[5]</sup>	219 <sup>[6]</sup>		
Units: days				
arithmetic mean (standard deviation)	-4 (± 5.7)	-3.7 (± 5.7)		

Notes:

[5] - FAS

[6] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in Number of Days With Pelvic Pain During Unscheduled Bleeding

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in Number of Days With Pelvic Pain During Unscheduled Bleeding
End point description: Evaluated was the number of days with bleeding-associated pelvic pain, excluding days during withdrawal bleeding (WB) and the 2 days preceding such WB, and during administration deviation bleeding and the 2 days preceding such bleeding (normalized to a standard 56-day period). Baseline period: 2 days before first menstrual bleeding until 3rd day before 3rd menstrual bleeding (normalized to standard 56-day period). Treatment period: 2 days before WB of the 1st treatment cycle until 3rd day before the WB of the cycle after the 2nd treatment cycle (normalized to standard 56-day period).	
End point type	Secondary
End point timeframe: Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[7]</sup>	219 <sup>[8]</sup>		
Units: days				
arithmetic mean (standard deviation)	0.3 (± 2.6)	0.1 (± 2)		

Notes:

[7] - FAS

[8] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in Rescue Medication Use (Only Bleeding Episodes Used Including the Two Days Before the Episode)

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in Rescue Medication Use (Only Bleeding Episodes Used Including the Two Days Before the Episode)
End point description: Rescue medication use was standardized intake of 200 mg Ibuprofen tablets. Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).	
End point type	Secondary
End point timeframe: Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[9]</sup>	219 <sup>[10]</sup>		
Units: tablets				
arithmetic mean (standard deviation)	-6.2 (± 14.8)	-6.6 (± 12.3)		

Notes:

[9] - FAS

[10] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change Between Baseline Evaluation Period and Treatment Evaluation Period in Rescue Medication Use (Entire Evaluation Period Used)

End point title	Change Between Baseline Evaluation Period and Treatment Evaluation Period in Rescue Medication Use (Entire Evaluation Period Used)
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End point description:

Rescue medication use was standardized intake of 200 mg Ibuprofen tablets. Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).

End point type	Secondary
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End point timeframe:

Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[11]</sup>	219 <sup>[12]</sup>		
Units: tablets				
arithmetic mean (standard deviation)	-4.5 (± 19.9)	-5.6 (± 14.3)		

Notes:

[11] - FAS

[12] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Interference of Dysmenorrheic Pain With Work/School and Social or Other Activity (Only Bleeding Episodes Used Including the Two Days Before)

End point title	Percentage of Subjects With Interference of Dysmenorrheic Pain With Work/School and Social or Other Activity (Only Bleeding Episodes Used Including the Two Days Before)
End point description: Interference of dysmenorrheic pain with work/school and social or other activity was assessed (yes/no). Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).	
End point type	Secondary
End point timeframe: Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[13]</sup>	230 <sup>[14]</sup>		
Units: percentage of subjects				
number (not applicable)				
Baseline period-daily activities impaired	92.3	91.3		
Baseline period- leisure activities impaired	90.6	89.6		
Treatment period-daily activities impaired	51.7	56.5		
Treatment period- leisure activities impaired	47.9	56.5		

Notes:

[13] - FAS

[14] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Interference of Dysmenorrheic Pain With Work/School and Social or Other Activity (Entire Evaluation Period Used)

End point title	Percentage of Subjects With Interference of Dysmenorrheic Pain With Work/School and Social or Other Activity (Entire Evaluation Period Used)
End point description: Interference of dysmenorrheic pain with work/school and social or other activity was assessed (yes/no). Baseline period: 2 days before the first menstrual bleeding until 3rd day before the 3rd menstrual bleeding (normalized to a standard 56-day period). Treatment period: 2 days before the withdrawal bleeding (WB) of the 1st evaluable treatment cycle until 3rd day before the WB of the cycle after the 2nd evaluable treatment cycle (normalized to a standard 56-day period).	
End point type	Secondary
End point timeframe: Baseline period (2 baseline cycles, usually 56 days) vs. treatment period (on-treatment cycles 2 and 3, usually 56 days)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[15]</sup>	230 <sup>[16]</sup>		
Units: percentage of subjects				
number (not applicable)				
Baseline period-daily activities impaired	93.2	92.2		
Baseline period- leisure activities impaired	92.3	90		
Treatment period-daily activities impaired	54.7	60		
Treatment period- leisure activities impaired	52.6	61.3		

Notes:

[15] - FAS

[16] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Satisfied With Study Treatment

End point title	Percentage of Subjects Satisfied With Study Treatment
End point description:	
Subjects were asked to express the degree of their satisfaction with study treatment.	
End point type	Secondary
End point timeframe:	
From cycle 1 to cycle 3 (28 days per cycle)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225 <sup>[17]</sup>	216 <sup>[18]</sup>		
Units: percentage of subjects				
number (not applicable)				
Missing	0.9	1.3		
Very satisfied	53.4	50.4		
Satisfied	32.1	30		
Neither satisfied nor dissatisfied	7.3	8.3		
Dissatisfied	2.1	3.5		
Very dissatisfied	0.4	0.4		

Notes:

[17] - FAS

[18] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Days With Bleeding or Spotting

End point title	Number of Days With Bleeding or Spotting
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe: From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[19]</sup>	197 <sup>[20]</sup>		
Units: days				
arithmetic mean (standard deviation)	20 (± 8.8)	23.6 (± 9.7)		

Notes:

[19] - FAS

[20] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Episodes With Bleeding or Spotting

End point title	Number of Episodes With Bleeding or Spotting
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe: From day 1 to day 90	



End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[21]</sup>	197 <sup>[22]</sup>		
Units: episodes				
arithmetic mean (standard deviation)	3.9 (± 1)	4.1 (± 0.8)		

Notes:

[21] - FAS

[22] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Length of Bleeding or Spotting Episodes

End point title	Mean Length of Bleeding or Spotting Episodes
End point description:	
Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe:	
From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[23]</sup>	197 <sup>[24]</sup>		
Units: days				
arithmetic mean (standard deviation)	5.17 (± 2.26)	5.83 (± 2.35)		

Notes:

[23] - FAS

[24] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Length of Bleeding or Spotting Episodes

End point title	Maximum Length of Bleeding or Spotting Episodes
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe: From day 1 to day 90	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[25]</sup>	197 <sup>[26]</sup>		
Units: days				
arithmetic mean (standard deviation)	7.1 (± 3.8)	8.4 (± 5.6)		

Notes:

[25] - FAS

[26] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Difference in Duration Between Longest and Shortest Bleeding or Spotting Episode

End point title	Difference in Duration Between Longest and Shortest Bleeding or Spotting Episode
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe: From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[27]</sup>	197 <sup>[28]</sup>		
Units: days				
arithmetic mean (standard deviation)	3.6 (± 3.6)	4.6 (± 5.6)		

Notes:

[27] - FAS

[28] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Days With Spotting-only

End point title	Number of Days With Spotting-only
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End point description:

Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.

End point type	Secondary
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End point timeframe:

From day 1 to day 90

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[29]</sup>	197 <sup>[30]</sup>		
Units: days				
arithmetic mean (standard deviation)	7.3 (± 6.9)	7.6 (± 7.5)		

Notes:

[29] - FAS

[30] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Episodes With Spotting-only

End point title	Number of Episodes With Spotting-only
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End point description:

Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90

days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.

End point type	Secondary
End point timeframe:	
From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201 <sup>[31]</sup>	197 <sup>[32]</sup>		
Units: episodes				
arithmetic mean (standard deviation)	0.5 (± 0.8)	0.4 (± 0.7)		

Notes:

[31] - FAS

[32] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Length of Spotting Only Episodes

End point title	Mean Length of Spotting Only Episodes
End point description:	
Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe:	
From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67 <sup>[33]</sup>	51 <sup>[34]</sup>		
Units: days				
arithmetic mean (standard deviation)	3.29 (± 2.39)	3.26 (± 2.79)		

Notes:

[33] - FAS

[34] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Length of Spotting Only Episodes

End point title	Maximum Length of Spotting Only Episodes
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary
End point timeframe: From day 1 to day 90	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67 <sup>[35]</sup>	51 <sup>[36]</sup>		
Units: days				
arithmetic mean (standard deviation)	3.9 (± 3.1)	3.6 (± 3)		

Notes:

[35] - FAS

[36] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Difference in Duration Between Longest and Shortest Spotting Only Episode

End point title	Difference in Duration Between Longest and Shortest Spotting Only Episode
End point description: Bleeding/spotting episodes (day[s] with bleeding/spotting preceded and followed by at least 2 bleeding/spotting-free days) were described using the reference period (RP) method (length of RP: 90 days) recommended by the World Health Organization. 1st RP started on the 1st day of study medication. The total number of days during bleeding or spotting episodes was counted. Spotting = less than associated with normal menstruation relative to the subject's experience with no need for sanitary protection (except for panty liners). Bleeding = any bleeding of greater intensity than spotting.	
End point type	Secondary

End point timeframe:

From day 1 to day 90

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67 <sup>[37]</sup>	51 <sup>[38]</sup>		
Units: days				
arithmetic mean (standard deviation)	1.2 (± 2.5)	0.7 (± 1.5)		

Notes:

[37] - FAS

[38] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Withdrawal Bleeding at Cycle 1

End point title	Percentage of Subjects With Withdrawal Bleeding at Cycle 1
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End point description:

Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[39]</sup>	222 <sup>[40]</sup>		
Units: percentage of subjects				
number (not applicable)	91.2	93.2		

Notes:

[39] - FAS

[40] - FAS

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Withdrawal Bleeding at Cycle 3

End point title	Percentage of Subjects With Withdrawal Bleeding at Cycle 3
-----------------	--

End point description:

Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 3 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204 <sup>[41]</sup>	198 <sup>[42]</sup>		
Units: percentage of subjects				
number (not applicable)	68.1	79.3		

Notes:

[41] - FAS

[42] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Length of Withdrawal Bleeding Episodes at Cycle 1

End point title	Length of Withdrawal Bleeding Episodes at Cycle 1
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End point description:

Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206 <sup>[43]</sup>	207 <sup>[44]</sup>		
Units: days				

arithmetic mean (standard deviation)	5.2 ( $\pm$ 2.7)	5.4 ( $\pm$ 2.4)		
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Notes:

[43] - FAS

[44] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Length of Withdrawal Bleeding Episodes at Cycle 3

End point title	Length of Withdrawal Bleeding Episodes at Cycle 3
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End point description:

Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 3 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139 <sup>[45]</sup>	157 <sup>[46]</sup>		
Units: days				
arithmetic mean (standard deviation)	4.5 ( $\pm$ 1.7)	5.2 ( $\pm$ 2)		

Notes:

[45] - FAS

[46] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Intensity of Withdrawal Bleeding Episodes at Cycle 1

End point title	Maximum Intensity of Withdrawal Bleeding Episodes at Cycle 1
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End point description:

Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. Intensity was defined as: 1 = none, 2 = spotting, 3 = light, 4 = normal, 5 = heavy.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)



End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206 <sup>[47]</sup>	207 <sup>[48]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	3.7 (± 1)	4 (± 0.9)		

Notes:

[47] - FAS

[48] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Intensity of Withdrawal Bleeding Episodes at Cycle 3

End point title	Maximum Intensity of Withdrawal Bleeding Episodes at Cycle 3
End point description:	
Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. Intensity was defined as: 1 = none, 2 = spotting, 3 = light, 4 = normal, 5 = heavy.	
End point type	Secondary
End point timeframe:	
At cycle 3 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139 <sup>[49]</sup>	157 <sup>[50]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	3.7 (± 0.8)	4.1 (± 0.8)		

Notes:

[49] - FAS

[50] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Onset of Withdrawal Bleeding Episodes at Cycle 1

End point title	Onset of Withdrawal Bleeding Episodes at Cycle 1
End point description: Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.	
End point type	Secondary
End point timeframe: At cycle 1 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206 <sup>[51]</sup>	207 <sup>[52]</sup>		
Units: days				
arithmetic mean (standard deviation)	4.8 (± 7)	4.9 (± 5.9)		

Notes:

[51] - FAS

[52] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Onset of Withdrawal Bleeding Episodes at Cycle 3

End point title	Onset of Withdrawal Bleeding Episodes at Cycle 3
End point description: Withdrawal bleeding was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.	
End point type	Secondary
End point timeframe: At cycle 3 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139 <sup>[53]</sup>	157 <sup>[54]</sup>		
Units: days				
arithmetic mean (standard deviation)	3.1 (± 3.7)	4.3 (± 4.4)		

Notes:

[53] - FAS

[54] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Intracyclic Bleeding at Cycle 1

End point title	Percentage of Subjects With Intracyclic Bleeding at Cycle 1
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End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[55]</sup>	222 <sup>[56]</sup>		
Units: percentage of subjects				
number (not applicable)	19	16.7		

Notes:

[55] - FAS

[56] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Intracyclic Bleeding at Cycle 3

End point title	Percentage of Subjects With Intracyclic Bleeding at Cycle 3
-----------------	---

End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 3 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204 <sup>[57]</sup>	198 <sup>[58]</sup>		
Units: percentage of subjects				
number (not applicable)	10.8	11.6		

Notes:

[57] - FAS

[58] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Intracyclic Bleeding Episodes at Cycle 1

End point title	Number of Intracyclic Bleeding Episodes at Cycle 1
End point description:	
Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.	
End point type	Secondary
End point timeframe:	
At cycle 1 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[59]</sup>	222 <sup>[60]</sup>		
Units: episodes				
arithmetic mean (standard deviation)	0.2 (± 0.5)	0.2 (± 0.4)		

Notes:

[59] - FAS

[60] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Intracyclic Bleeding Episodes at Cycle 3

End point title	Number of Intracyclic Bleeding Episodes at Cycle 3
End point description:	
Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.	
End point type	Secondary
End point timeframe:	
At cycle 3 (28 days per cycle)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204 <sup>[61]</sup>	198 <sup>[62]</sup>		
Units: episodes				
arithmetic mean (standard deviation)	0.1 (± 0.3)	0.1 (± 0.4)		

Notes:

[61] - FAS

[62] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Length of Intracyclic Bleeding Episodes at Cycle 1

End point title	Maximum Length of Intracyclic Bleeding Episodes at Cycle 1
End point description:	
Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.	
End point type	Secondary
End point timeframe:	
At cycle 1 (28 days per cycle)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 <sup>[63]</sup>	37 <sup>[64]</sup>		
Units: days				
arithmetic mean (standard deviation)	6 (± 5.4)	6.2 (± 5.7)		

Notes:

[63] - FAS

[64] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Length of Intracyclic Bleeding Episodes at Cycle 3

End point title	Maximum Length of Intracyclic Bleeding Episodes at Cycle 3
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End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal.

End point type	Secondary
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End point timeframe:

At cycle 3 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 <sup>[65]</sup>	23 <sup>[66]</sup>		
Units: days				
arithmetic mean (standard deviation)	5.5 (± 4.7)	4.9 (± 4.1)		

Notes:

[65] - FAS

[66] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Intracyclic Bleeding Days at Cycle 1

End point title	Number of Intracyclic Bleeding Days at Cycle 1
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End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. The total number of days during intracyclic bleeding episodes was counted.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[67]</sup>	222 <sup>[68]</sup>		
Units: days				
arithmetic mean (standard deviation)	1.2 (± 3.5)	1 (± 3.3)		

Notes:

[67] - FAS

[68] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Intracyclic Bleeding Days at Cycle 3

End point title	Number of Intracyclic Bleeding Days at Cycle 3
End point description:	
Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. The total number of days during intracyclic bleeding episodes was counted.	
End point type	Secondary
End point timeframe:	
At cycle 3 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204 <sup>[69]</sup>	198 <sup>[70]</sup>		
Units: days				
arithmetic mean (standard deviation)	0.6 (± 2.3)	0.6 (± 2.1)		

Notes:

[69] - FAS

[70] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Maximum Intensity of Intracyclic Bleeding

## Episodes at Cycle 1

End point title	Percentage of Subjects With Maximum Intensity of Intracyclic Bleeding Episodes at Cycle 1
-----------------	---

End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. Intensity could be described as spotting, light, normal or heavy.

End point type	Secondary
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End point timeframe:

At cycle 1 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43 <sup>[71]</sup>	37 <sup>[72]</sup>		
Units: percentage of subjects				
number (not applicable)				
Spotting	53.5	62.2		
Light	30.2	10.8		
Normal	9.3	13.5		
Heavy	7	13.5		

Notes:

[71] - FAS

[72] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Maximum Intensity of Intracyclic Bleeding Episodes at Cycle 3

End point title	Percentage of Subjects With Maximum Intensity of Intracyclic Bleeding Episodes at Cycle 3
-----------------	---

End point description:

Intracyclic bleeding episodes were any bleeding episodes not qualifying as withdrawal bleeding. The latter was defined as the first bleeding episode after complete or partial progestogen withdrawal (i.e. the first episode starting after the last day of progestogen intake). If a bleeding episode was ongoing on the last day of progestogen intake and the following day, this episode was regarded as the withdrawal bleeding episode, as long as it had started not more than 4 days before the progestogen withdrawal. Intensity could be described as spotting, light, normal or heavy.

End point type	Secondary
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End point timeframe:

At cycle 3 (28 days per cycle)



<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 <sup>[73]</sup>	23 <sup>[74]</sup>		
Units: percentage of subjects				
number (not applicable)				
Spotting	45.5	30.4		
Light	27.3	21.7		
Normal	13.6	30.4		
Heavy	13.6	17.4		

Notes:

[73] - FAS

[74] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Screening

End point title	Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Screening
-----------------	--

End point description:

The investigator was asked to interview the subject and record the number of missed hours/days from work due to dysmenorrheic pain in the previous menstrual cycle.

End point type	Secondary
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End point timeframe:

At screening (28 days)

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[75]</sup>	230 <sup>[76]</sup>		
Units: percentage of subjects				
number (not applicable)				
Missing	0.4	0		
Never	38	40.4		
4 working hours	16.2	16.1		
1 working day	26.5	29.6		
>= 2 working days	18.8	13.9		

Notes:

[75] - FAS

[76] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Baseline Cycle

End point title	Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Baseline Cycle
End point description: The investigator was asked to interview the subject and record the number of missed hours/days from work due to dysmenorrheic pain in the previous menstrual cycle.	
End point type	Secondary
End point timeframe: At Baseline (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[77]</sup>	229 <sup>[78]</sup>		
Units: percentage of subjects				
number (not applicable)				
Missing	0	0		
Never	47.9	51.7		
4 working hours	13.2	11.7		
1 working day	20.9	23.9		
>= 2 working days	17.9	12.2		

Notes:

[77] - FAS

[78] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Cycle 2

End point title	Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Cycle 2
End point description: The investigator was asked to interview the subject and record the number of missed hours/days from work due to dysmenorrheic pain in the previous menstrual cycle.	
End point type	Secondary
End point timeframe: At cycle 2 (28 days per cycle)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224 <sup>[79]</sup>	212 <sup>[80]</sup>		
Units: percentage of subjects				
number (not applicable)				
Missing	0	0		
Never	78.6	72.6		
4 working hours	8.5	6.5		
1 working day	6.4	8.7		
>= 2 working days	2.1	4.3		

Notes:

[79] - FAS

[80] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Final Examination

End point title	Percentage of Subjects Missing Time From Work Due to Dysmenorrheic Pain at Final Examination
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End point description:

The investigator was asked to interview the subject and record the number of missed hours/days from work due to dysmenorrheic pain in the previous menstrual cycle.

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[81]</sup>	217 <sup>[82]</sup>		
Units: percentage of subjects				
number (not applicable)				
Missing	0.4	0		
Never	85.9	85.2		
4 working hours	5.6	2.6		
1 working day	3	4.8		
>= 2 working days	1.7	1.7		

Notes:

[81] - FAS

[82] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Own Costs of Physiotherapy Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Physiotherapy Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of physiotherapy per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 <sup>[83]</sup>	174 <sup>[84]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[83] - FAS

[84] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Own Costs of Pain Medication Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Pain Medication Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of pain medication per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206 <sup>[85]</sup>	195 <sup>[86]</sup>		
Units: dollars				
median (full range (min-max))	5.46 (0 to 30)	5.04 (0 to 27.49)		

Notes:

[85] - FAS

[86] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Own Costs of Vitamins Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Vitamins Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of vitamins per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173 <sup>[87]</sup>	176 <sup>[88]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 65.45)	0 (0 to 65.45)		

Notes:

[87] - FAS

[88] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Own Costs of Massages Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Massages Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of

massages per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
End point timeframe:	
At screening (average over 3 months before screening)	

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172 <sup>[89]</sup>	172 <sup>[90]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 60)	0 (0 to 295.98)		

Notes:

[89] - FAS

[90] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Own Costs of Acupuncture Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Acupuncture Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of acupuncture per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174 <sup>[91]</sup>	174 <sup>[92]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 150)	0 (0 to 74)		

Notes:

[91] - FAS

[92] - FAS

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Own Costs of Medical Counseling Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire**

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End point title	Own Costs of Medical Counseling Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of medical counseling per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

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End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170 <sup>[93]</sup>	170 <sup>[94]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 271.68)	0 (0 to 98.17)		

Notes:

[93] - FAS

[94] - FAS

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Own Costs of Alternative Medicine Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire**

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End point title	Own Costs of Alternative Medicine Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
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End point description:

The subjects were asked to complete a resource use questionnaire indicating their other own costs of alternative medicine per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

End point type	Secondary
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End point timeframe:

At screening (average over 3 months before screening)

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End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177 <sup>[95]</sup>	175 <sup>[96]</sup>		

Units: dollars				
median (full range (min-max))	0 (0 to 196.34)	0 (0 to 110)		

Notes:

[95] - FAS

[96] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Own Costs of Herbs/Teas Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Own Costs of Herbs/Teas Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
-----------------	---

End point description:

The subjects were asked to complete a resource use questionnaire indicating their own costs of herbs/teas per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

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

End point timeframe:

At screening (average over 3 months before screening)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183 <sup>[97]</sup>	179 <sup>[98]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 30)	0 (0 to 10)		

Notes:

[97] - FAS

[98] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: Other Own Costs Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire

End point title	Other Own Costs Per Treatment Converted to U.S. Dollars as Measured by Resource Use Questionnaire
-----------------	---

End point description:

The subjects were asked to complete a resource use questionnaire indicating their other own costs per treatment of dysmenorrheic pain. Costs were converted to U.S. dollars.

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

End point timeframe:

At screening (average over 3 months before screening)



End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192 <sup>[99]</sup>	194 <sup>[100]</sup>		
Units: dollars				
median (full range (min-max))	0 (0 to 15)	0 (0 to 42)		

Notes:

[99] - FAS

[100] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects With Improvement in the Investigators' Assessment in the Clinical Global Impression

End point title	Subjects With Improvement in the Investigators' Assessment in the Clinical Global Impression
-----------------	--

End point description:

The Clinical Global Impression Scale (CGI) is a widely used rating scale/assessment instrument in psychopharmacology research in general, and in studies on women's health in particular. Investigators were asked to rate the subjects' improvement during the course of the study.

End point type	Secondary
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End point timeframe:

At cycle 2 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	223 <sup>[101]</sup>	210 <sup>[102]</sup>		
Units: subjects				
Missing	0	0		
Not assessed	1	1		
Very much improved	63	42		
Much improved	87	84		
Minimally improved	49	54		
No change	17	23		
Minimally worse	6	3		
Much worse	0	3		

Notes:

[101] - FAS

[102] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects With Improvement in Subjects' Assessment in the Clinical Global Impression

End point title	Subjects With Improvement in Subjects' Assessment in the Clinical Global Impression
-----------------	---

End point description:

The CGI is a widely used rating scale/assessment instrument in psychopharmacology research in general, and in studies on women's health in particular. Subjects were asked to rate their improvement during the course of the study.

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

End point timeframe:

At cycle 2 (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	223 <sup>[103]</sup>	210 <sup>[104]</sup>		
Units: subjects				
Missing	1	0		
Not assessed	1	1		
Very much improved	60	46		
Much improved	91	75		
Minimally improved	47	57		
No change	18	24		
Minimally worse	5	4		
Much worse	0	3		

Notes:

[103] - FAS

[104] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Physical Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Physical Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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**End point description:**

The standard questionnaire SF-36 version 1 (v1), a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

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

**End point timeframe:**

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[105]</sup>	229 <sup>[106]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	90.2 (± 16.7)	89.6 (± 17.5)		

**Notes:**

[105] - FAS

[106] - FAS

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Physical Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination**

End point title	Physical Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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**End point description:**

The standard questionnaire SF-36 v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

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

**End point timeframe:**

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[107]</sup>	217 <sup>[108]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	93.7 (± 14.2)	92.5 (± 15)		

Notes:

[107] - FAS

[108] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Social Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Social Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
-----------------	---

End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

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

End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[109]</sup>	229 <sup>[110]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	78.85 (± 18.99)	77.35 (± 20.56)		

Notes:

[109] - FAS

[110] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Social Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Social Functioning as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
End point timeframe:	
At final examination (28 days)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[111]</sup>	217 <sup>[112]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	85.95 (± 19.09)	84.79 (± 17.36)		

Notes:

[111] - FAS

[112] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mental Health as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Mental Health as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate patient populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
End point timeframe:	
At baseline cycle (28 days per cycle)	

<b>End point values</b>	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[113]</sup>	229 <sup>[114]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	73.6 (± 15.6)	72.6 (± 16.3)		

Notes:

[113] - FAS

[114] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mental Health as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Mental Health as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[115]</sup>	217 <sup>[116]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	77.3 (± 14.9)	76.4 (± 14.7)		

Notes:

[115] - FAS

[116] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Vitality as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Vitality as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
-----------------	---

End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

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

End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[117]</sup>	229 <sup>[118]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	62.6 (± 18)	62.2 (± 18.2)		

Notes:

[117] - FAS

[118] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Vitality as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Vitality as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[119]</sup>	217 <sup>[120]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	68.2 (± 17)	67.2 (± 16.8)		

Notes:

[119] - FAS

[120] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: General Health as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	General Health as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[121]</sup>	229 <sup>[122]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	75.8 (± 17.5)	72.7 (± 16.9)		

Notes:

[121] - FAS

[122] - FAS

## Statistical analyses

No statistical analyses for this end point

## Secondary: General Health as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	General Health as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[123]</sup>	217 <sup>[124]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	77.2 (± 17.9)	76.5 (± 16.6)		



Notes:

[123] - FAS

[124] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Role Physical as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Role Physical as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[125]</sup>	229 <sup>[126]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	77.8 (± 33.6)	79.4 (± 32.7)		

Notes:

[125] - FAS

[126] - FAS

## Statistical analyses

No statistical analyses for this end point

### Secondary: Role Physical as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Role Physical as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:  
At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[127]</sup>	217 <sup>[128]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	89.6 (± 23)	87.9 (± 25.9)		

Notes:

[127] - FAS

[128] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Role Emotional as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Role Emotional as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[129]</sup>	229 <sup>[130]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	81.91 (± 31.5)	79.18 (± 34.74)		

Notes:

[129] - FAS

[130] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Role Emotional as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Role Emotional as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[131]</sup>	217 <sup>[132]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	88.64 (± 26.36)	83.87 (± 30.28)		

Notes:

[131] - FAS

[132] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Bodily Pain as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle

End point title	Bodily Pain as Measured by General Health and Well-being Questionnaire SF-36 at Baseline Cycle
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At baseline cycle (28 days per cycle)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234 <sup>[133]</sup>	229 <sup>[134]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	50.7 (± 24.4)	51.8 (± 23)		

Notes:

[133] - FAS

[134] - FAS

### Statistical analyses

No statistical analyses for this end point

### Secondary: Bodily Pain as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination

End point title	Bodily Pain as Measured by General Health and Well-being Questionnaire SF-36 at Final Examination
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End point description:

The standard questionnaire SF-36v1, a general health status measure used to evaluate subject populations and to compare health status across different populations, was completed by subjects as a self-administered native language version. Percentages of absolute scores were calculated such that 0 represents the lowest possible score (worst outcome) and 100 the highest possible score (best outcome).

End point type	Secondary
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End point timeframe:

At final examination (28 days)

End point values	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	Ethinyl Estradiol, Levonorgestrel (Miranova)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226 <sup>[135]</sup>	217 <sup>[136]</sup>		
Units: scores on a scale				
arithmetic mean (standard deviation)	77 (± 21.5)	74 (± 22.1)		

Notes:

[135] - FAS

[136] - FAS

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From treatment period (on-treatment cycles 2 and 3, usually 56 days) up to end of study visit (visit 4, final examination, 28 days)

Adverse event reporting additional description:

Treatment-emergent adverse events were defined as adverse events/serious adverse events that started or worsened after the study drug treatment.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.1
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### Reporting groups

Reporting group title	Ethinyl Estradiol, Levonorgestrel (Miranova)
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Reporting group description:

Daily oral administration of one tablet placebo plus one tablet SH D593B (Miranova) for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.

Reporting group title	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)
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Reporting group description:

Daily oral administration of one tablet SH T00658ID (BAY86-5027) plus one tablet placebo for 28 days without tablet-free interval for 3 treatment cycles. Subjects who received treatment were included in baseline period.

Serious adverse events	Ethinyl Estradiol, Levonorgestrel (Miranova)	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 230 (0.87%)	2 / 234 (0.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 230 (0.43%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian torsion			
subjects affected / exposed	0 / 230 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Depression			
subjects affected / exposed	1 / 230 (0.43%)	0 / 234 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Helminthic infection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 234 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Ethinyl Estradiol, Levonorgestrel (Miranova)	Estradiol Valerate, Dienogest (Natazia, Qlaira, BAY86-5027)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 230 (53.04%)	131 / 234 (55.98%)	
Nervous system disorders			
Headache			
subjects affected / exposed	34 / 230 (14.78%)	32 / 234 (13.68%)	
occurrences (all)	55	55	
Tension headache			
subjects affected / exposed	9 / 230 (3.91%)	14 / 234 (5.98%)	
occurrences (all)	43	40	
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	3 / 230 (1.30%)	7 / 234 (2.99%)	
occurrences (all)	3	7	
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	2 / 230 (0.87%)	5 / 234 (2.14%)	
occurrences (all)	7	10	
Nausea			
subjects affected / exposed	5 / 230 (2.17%)	2 / 234 (0.85%)	
occurrences (all)	6	2	
Reproductive system and breast disorders			

Cervical dysplasia subjects affected / exposed occurrences (all)	9 / 230 (3.91%) 9	7 / 234 (2.99%) 7	
Dysfunctional uterine bleeding subjects affected / exposed occurrences (all)	5 / 230 (2.17%) 6	3 / 234 (1.28%) 4	
Dysmenorrhoea subjects affected / exposed occurrences (all)	82 / 230 (35.65%) 210	87 / 234 (37.18%) 208	
Metrorrhagia subjects affected / exposed occurrences (all)	13 / 230 (5.65%) 17	18 / 234 (7.69%) 28	
Cervix inflammation subjects affected / exposed occurrences (all)	4 / 230 (1.74%) 4	9 / 234 (3.85%) 9	
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	5 / 230 (2.17%) 5	2 / 234 (0.85%) 2	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 230 (3.04%) 10	4 / 234 (1.71%) 6	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2009	Amendment 1 was globally implemented before the inclusion of the first subject in the study. As an adequate (re-)supply for the originally planned comparator (Alesse) was not considered feasible, Alesse was replaced by SH D593B (Miranova), and the originally intended encapsulation of tablets for blinding was replaced by a double-dummy design that was considered to have advantages for the subjects, study drug supply and the study as a whole.
26 August 2009	Amendment 2 was globally implemented to reflect revised rules to be observed in case of missed tablets to further improve readability. These revised rules had been submitted with the regulatory submission of SH T00658ID to the Food and Drug Administration (FDA) on 02 Jul 2009. In addition, according to the general recommendations for combined oral contraceptive users, the maximum age for smokers to be eligible for this study was changed from 30 to 35 years.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported