



## Clinical trial results: How common are mood and sexual side-effects from combined oral contraceptives?

### Summary

EudraCT number	2013-000925-30
Trial protocol	SE
Global end of trial date	29 September 2015

### Results information

Result version number	v1 (current)
This version publication date	22 March 2020
First version publication date	22 March 2020
Summary attachment (see zip file)	COCs and Mood, article published in Psychoneuroendocrinology (CL PNEC.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	10
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#### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Uppsala University
Sponsor organisation address	Uppsala University Hospital, Uppsala, Sweden,
Public contact	Inger Sundström Poromaa, Uppsala University, 46 186115764, inger.sundstrom@kbh.uu.se
Scientific contact	Inger Sundström Poromaa, Uppsala University, 46 186115764, inger.sundstrom@kbh.uu.se

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2015
Global end of trial reached?	Yes
Global end of trial date	29 September 2015
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

to prospectively estimate the prevalence of mood and sexual side effects in combined oral contraceptives users  
to compare the severity of mood and sexual side effects between combined oral contraceptives users and placebo users

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Protection of trial subjects:

The study participants underwent pregnancy tests on the screening visit, and then before the start of each treatment cycle. At the visits during ongoing treatment as well as at the follow-up, the study participants were asked for any adverse events.

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Background therapy: -

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Evidence for comparator: -

Actual start date of recruitment	09 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Sweden: 202
Worldwide total number of subjects	202
EEA total number of subjects	202

Notes:

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**Subjects enrolled per age group**

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In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	202
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited by advertisements in local newspapers, on local notice boards and students websites. Recruitment started in September 2013 and ended in May 2015. Participants were recruited from six cities in Sweden.

### Pre-assignment

Screening details:

A total of 224 subjects were screened for the study. Following a screening visit, women kept daily symptom diaries for one menstrual cycle (baseline cycle). After the baseline cycle, women started taking a combined oral contraceptive or placebo tablets once daily during three treatment cycles.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

After the baseline cycle was completed, women started taking active treatment (COC) or placebo capsules once daily on the first day of menses and continued treatment for 24 days, followed by four pill-free days.

<b>Arm title</b>	1.5 mg oestradiol/2.5 mg nomegestrolacetate
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Combined oral contraceptive
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

After the baseline cycle, women started taking active treatment (COC) or placebo once daily on the first day of menses and continued treatment for 24 days, followed by 4 pill-free days, repeated in three treatment cycles.

Number of subjects in period 1	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate
Started	100	102
Completed	94	84
Not completed	6	18
Consent withdrawn by subject	4	7
Adverse event, non-fatal	-	5
Pregnancy	1	-
Unknown	-	3
Lost to follow-up	1	3

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	1.5 mg oestradiol/2.5 mg nomegestrolacetate
Reporting group description: -	

<b>Reporting group values</b>	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate	Total
Number of subjects	100	102	202
Age categorical Units: Subjects			
Adults (18-64 years)	100	102	202
Age continuous Units: years			
arithmetic mean	24.8	23.8	
standard deviation	± 4.2	± 4.2	-
Gender categorical Units: Subjects			
Female	100	102	202
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	1.5 mg oestradiol/2.5 mg nomegestrolacetate
Reporting group description: -	

### Primary: Change in mood scores

End point title	Change in mood scores
End point description: Mood was scored on Daily Rating of Severity of Symptoms (DRSP) daily during baseline (hormonal free) and the third treatment cycle and any change and compared after end of trial. The DRSP consists of 21 items that reflect symptoms such as irritability, mood swings and fatigue. Each item is scored on 6-point Likert scale, with 6 representing maximum severity and 1 representing complete absence of a particular symptom.	
End point type	Primary
End point timeframe: 3 months	

End point values	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	84		
Units: 1-6	94	84		

### Statistical analyses

Statistical analysis title	Change in MFSQ
Statistical analysis description: Delta scores were calculated for the MFSQ domains as difference between the final treatment cycle and baseline, meaning that negative delta scores indicate worsening and positive delta scores indicated improvement. Baseline and delta scores were compared between treatment groups by Mann-Whitney U-test.	
Comparison groups	Placebo v 1.5 mg oestradiol/2.5 mg nomegestrolacetate
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	$\leq 0.05$
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

<b>Statistical analysis title</b>	Change in mood scores
Comparison groups	Placebo v 1.5 mg oestradiol/2.5 mg nomegestrolacetate
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA

### Primary: Change in MFSQ scores

End point title	Change in MFSQ scores
End point description:	Change in McCoy Female Sexuality Questionnaire during last treatment cycle compared to baseline. The questionnaire consists of 19 questions, answered using a 7-point Likert scale where 1 represents negative answers such as "not at all enjoyable" and 7 represents positive answers such as "very enjoyable".
End point type	Primary
End point timeframe:	3 months

<b>End point values</b>	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	84		
Units: 1-7	94	84		

### Statistical analyses

<b>Statistical analysis title</b>	Change in sexual function
Comparison groups	Placebo v 1.5 mg oestradiol/2.5 mg nomegestrolacetate
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Four months

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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### Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	1.5 mg oestradiol/2.5 mg nomegestrolacetate
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Reporting group description: -

<b>Serious adverse events</b>	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	0 / 102 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

<b>Non-serious adverse events</b>	Placebo	1.5 mg oestradiol/2.5 mg nomegestrolacetate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 100 (21.00%)	34 / 102 (33.33%)	
Reproductive system and breast disorders			
Bleeding disturbances			
subjects affected / exposed	11 / 100 (11.00%)	26 / 102 (25.49%)	
occurrences (all)	11	26	
Sexual function decrease			
subjects affected / exposed	3 / 100 (3.00%)	13 / 102 (12.75%)	
occurrences (all)	3	13	
Breast swelling			

subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5	8 / 102 (7.84%) 8	
Dysmenorrhea subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6	2 / 102 (1.96%) 6	
Gastrointestinal disorders Change in appetite subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6	7 / 102 (6.86%) 7	
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 9	9 / 102 (8.82%) 9	
Psychiatric disorders Mood symptoms subjects affected / exposed occurrences (all)	21 / 100 (21.00%) 21	34 / 102 (33.33%) 34	Additional description: Any report of depressed mood, anxiety, irritability, mood swings, difficulties concentrating, or affect lability
Fatigue subjects affected / exposed occurrences (all)	7 / 100 (7.00%) 7	7 / 102 (6.86%) 7	

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported

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### **Online references**

<http://www.ncbi.nlm.nih.gov/pubmed/27923181>

<http://www.ncbi.nlm.nih.gov/pubmed/30352399>