Clinical trial results:
The effect of myoinositol (MI) or metformin treatment on symptoms of polycystisk ovary syndrome (PCOS), including metabolism, menstrual pattern, quality of life and mental health.

Summary

EudraCT number	2016-004506-34
Trial protocol	DK
Global end of trial date	29 October 2021

Results information

Result version number	v1 (current)
This version publication date	01 February 2023
First version publication date	01 February 2023

Trial information

Trial identification

Sponsor protocol code	16.022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Dorte Glintborg: Marianne Skovsager Andersen

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J.B. Winsløws Vej 4, Odense, Denmark, 5000
Public contact	Pernille Ravn, Odense Universitetshospital, 0045 28435625, pernille.ravn@rsyd.dk
Scientific contact	Pernille Ravn, Odense Universitetshospital, 0045 28435625, pernille.ravn@rsyd.dk

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	01 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2020
Global end of trial reached?	Yes
Global end of trial date	29 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of the dietary supplement myoinositol compared to the drug metformin in women with polycystic ovarian syndrome (PCOS). PCOS is characterized by irregular menstruations, high blood levels of male hormones, and increased male hair growth. Myoinositol and metformin decrease insulin resistance. The effect of myoinositol on symptoms of PCOS is not fully investigated and we investigate the effect compared to standard treatment with metformin. In the trial we investigate the effect on anthropometric measures, glucose metabolism, blood lipids, mental health, quality of life, sex hormones, menstrual pattern and side effects.

Protection of trial subjects:

Participants gave written informed consent after oral and written information and time for consideration. The local Ethics committee and the Danish Medicines Agency approved the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	45
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We recruited participants through the PCOS outpatient clinic, Department of Gynecology and Obstetrics, Odense University Hospital, Denmark.

Pre-assignment

Screening details:

Inclusion criteria were: PCOS diagnosed according to the Rotterdam criteria (2) and age 18-50 years. Exclusion criteria were other causes of oligomenorrhea and/or hirsutism, including abnormal values of prolactin, TSH or 17-OH progesterone, postmenopausal values of FSH (>25 IE/l), type 2 diabetes (HbA1c > 48 mmol/mol) or type 1 diabetes.

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Myoinositol (MI)

Arm description:

MI was administered as one sachet of 2 mg MI and 200 mg Folic acid twice daily.

Arm type	Experimental
Investigational medicinal product name	Myoinositol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral solution
Routes of administration	Oral use

Dosage and administration details:

Myoinositol 2 mg and Folic acid 200 mg in one sachet, twice daily.

Arm title	Metformin (MET)

Arm description:

MET was administered as tablets of 500 mg and dose was one tablet twice daily for two weeks and two tablets twice daily hereafter.

Arm type	Active comparator
Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Metformin was administered as tablets of 500 mg; one tablet twice daily for two weeks, and hereafter two tablets twice daily.

Number of subjects in period 1	Myoinositol (MI)	Metformin (MET)
Started	22	23
Completed	16	12
Not completed	6	11
Adverse event, non-fatal	1	5
Pregnancy	-	4
Lost to follow-up	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Myoinositol (MI)
Reporting group description:	
MI was administered as one sachet of 2 mg MI and 200 mg Folic acid twice daily.	
Reporting group title	Metformin (MET)
Reporting group description:	
MET was administered as tablets of 500 mg and dose was one tablet twice daily for two weeks and two tablets twice daily hereafter.	

Reporting group values	Myoinositol (MI)	Metformin (MET)	Total
Number of subjects	22	23	45
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	25	27	
inter-quartile range (Q1-Q3)	22 to 34	24 to 33	-
Gender categorical			
Units: Subjects			
Female	22	23	45
Male	0	0	0
Cycle length			
Units: days			
median	45	47	
inter-quartile range (Q1-Q3)	35 to 175	35 to 82	-
BMI			
Units: kg/m^2			
median	34.2	35.2	
inter-quartile range (Q1-Q3)	30.9 to 37.2	31.0 to 39.8	-

End points

End points reporting groups

Reporting group title	Myoinositol (MI)
Reporting group description: MI was administered as one sachet of 2 mg MI and 200 mg Folic acid twice daily.	
Reporting group title	Metformin (MET)
Reporting group description: MET was administered as tablets of 500 mg and dose was one tablet twice daily for two weeks and two tablets twice daily hereafter.	

Primary: HOMA-IR

End point title	HOMA-IR
End point description:	
End point type	Primary
End point timeframe: Baseline values	

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: pmol mmol l^-2				
median (inter-quartile range (Q1-Q3))	28.5 (19.6 to 45.6)	30.9 (24.9 to 32.4)		

Statistical analyses

Statistical analysis title	Statistical analysis plan
Statistical analysis description: Mann-Whitney U test was used to compare baseline data and delta-values (6-0 months) MI vs. MET. Wilcoxon Signed-Rank test was used to test within-group changes in MI and MET groups. Statistical analysis used for all endpoints.	
Comparison groups	Metformin (MET) v Myoinositol (MI)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: SF-36

End point title	SF-36

End point description:

End point type	Secondary

End point timeframe:

Baseline values

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))				
Physical functioning	90 (75 to 95)	90 (85 to 95)		
Role limitations due to physical health	88 (50 to 100)	100 (75 to 100)		
Role limitations due to emotional problems	100 (0 to 100)	100 (50 to 100)		
Energy/fatigue	50 (35 to 60)	40 (25 to 65)		
Emotional well-being	74 (60 to 84)	72 (58 to 84)		
Social functioning	59 (45 to 80)	53 (36 to 73)		
Pain	58 (45 to 90)	74 (68 to 95)		
General health	65 (50 to 80)	58 (38 to 80)		

Statistical analyses

No statistical analyses for this end point

Secondary: HDL

End point title	HDL

End point description:

High-density Lipoprotein

End point type	Secondary

End point timeframe:

Baseline values

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	1.2 (1.0 to 1.3)	1.3 (1.2 to 1.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin (fasting)

End point title	Insulin (fasting)

End point description:

End point type	Secondary

End point timeframe:

Baseline values

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: pmol/L				
median (inter-quartile range (Q1-Q3))	126 (85 to 190)	117 (112 to 143)		

Statistical analyses

No statistical analyses for this end point

Secondary: Glucose (fasting)

End point title	Glucose (fasting)

End point description:

End point type	Secondary

End point timeframe:

Baseline values

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))	5.2 (5.0 to 5.4)	5.3 (5.1 to 5.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: BMI

End point title	BMI
End point description: Body Mass Index	
End point type	Secondary
End point timeframe: Basline values	

End point values	Myoinositol (MI)	Metformin (MET)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	12		
Units: kg/m2				
median (inter-quartile range (Q1-Q3))	34.2 (30.9 to 37.2)	35.2 (31.0 to 39.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study till end.	
Assessment type	Systematic
Dictionary used	
Dictionary name	ICD10
Dictionary version	ICD10
Reporting groups	
Reporting group title	Myoinositol (MI)
Reporting group description:	
MI was administered as one sachet of 2 mg MI and 200 mg Folic acid twice daily.	
Reporting group title	Metformin (MET)
Reporting group description:	
MET was administered as tablets of 500 mg and dose was one tablet twice daily for two weeks and two tablets twice daily hereafter.	

Serious adverse events	Myoinositol (MI)	Metformin (MET)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 23 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Myoinositol (MI)	Metformin (MET)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 22 (18.18%)	16 / 23 (69.57%)	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	2 / 22 (9.09%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Mood swings			
subjects affected / exposed	0 / 22 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Increased body hair			

subjects affected / exposed	0 / 22 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Gastrointestinal adverse events	Additional description: Nausea, diarrhoea, vomiting and opstipation.		
subjects affected / exposed	1 / 22 (4.55%)	12 / 23 (52.17%)	
occurrences (all)	1	12	
Reproductive system and breast disorders			
Irregular menstrual cycle			
subjects affected / exposed	1 / 22 (4.55%)	0 / 23 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported