Clinical trial results:
A randomised controlled trial to compare the effect of micronized progesterone and Medroxyprogesterone Acetate on the vascular elasticity, lipid profile and coagulation cascade of women with premature ovarian failure.

Summary

EudraCT number	2012-004511-30
Trial protocol	GB
Global end of trial date	23 September 2016

Results information

Result version number	v1 (current)
This version publication date	29 July 2019
First version publication date	29 July 2019
Summary attachment (see zip file)	FINAL STUDY REPORT (Clinical Study Report POF01 Final 02Jul19.pdf)

Trial information

Trial identification

Sponsor protocol code	POF01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College Hospital NHS Foundation Trust
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE5 9RS
Public contact	Haitham Hamoda, King's College Hospital NHS Foundation Trust, 0044 02032995390, haitham.hamoda@nhs.net
Scientific contact	Haitham Hamoda, King's College Hospital NHS Foundation Trust, 0044 02032995390, haitham.hamoda@nhs.net

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	23 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2016
Global end of trial reached?	Yes
Global end of trial date	23 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
To assess the effect of micronized progesterone and medroxy progesterone acetate on vascular elasticity. This will be assessed by examining the changes in pulse wave analysis in women with premature ovarian failure receiving combined oestrogen/progestogen HRT.

Protection of trial subjects:

Prior to randomisation, the participants will be asked to stop their current treatment regimen for a total of 1 month, to ensure an adequate washout time period has been accounted for. This washout time frame has been based on other published trials. It accounts for the half life of the medication. It is necessary to ensure that previous treatments do not influence or impact on the trial results. There is no evidence to suggest any risk from stopping their current treatment regime for this short duration.

Background therapy:

Combined HRT is the recommended treatment in women with POI until the natural age of the menopause. There are many different varieties. This study assessed two different progesterone preparations given in combination with transdermal oestrogen.

If the subjects were previously prescribed HRT, then a wash out period of 4-6 weeks was advised prior to starting the new preparation.

Each treatment arm was prescribed a type of HRT as treatment is recommended. No patient was given a placebo.

Evidence for comparator: -

Actual start date of recruitment	02 January 2013
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 Kingdom: 68
Worldwide total number of subjects	68
EEA total number of subjects	68

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)	68
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from King's College London NHS Foundation Trust over a 30 month period between 2013 and 2016.

Pre-assignment

Screening details:

Prior to randomisation, the participants will be asked to stop their current treatment regimen for a total of 1 month, to ensure an adequate washout time period has been accounted for. There is no evidence to suggest any risk from stopping their current treatment regime for this short duration.

Period 1

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

Blinding implementation details:

Open label trial

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A - Utrogestan

Arm description:

Utrogestan, oral, 200 mg/24 hours from days 15-26 of a 28 days cycle.

Arm type	Experimental
Investigational medicinal product name	Utrogestan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Utrogestan, oral, 200 mg/24 hours from days 15-26 of a 28 days cycle.

Arm title	Group B - Provera

Arm description:

Medroxyprogesterone Acetate, Provera, oral, 10 mg/24 hours from days 16-26/cycle.

Arm type	Experimental
Investigational medicinal product name	Provera
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Medroxyprogesterone Acetate, Provera, oral, 10 mg/24 hours from days 16-26/cycle.

Number of subjects in period 1	Group A - Utrogestan	Group B - Provera
Started	34	34
Completed	28	31
Not completed	6	3
Consent withdrawn by subject	-	1
Patient choice	1	-
Protocol deviation	1	1
Lack of efficacy	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	68	68	
Age categorical Units: Subjects			
Adults (18-64 years)	68	68	
Gender categorical Units: Subjects			
Female	68	68	
Male	0	0	

End points

End points reporting groups

Reporting group title	Group A - Utrogestan
Reporting group description:	
Utrogestan, oral, 200 mg/24 hours from days 15-26 of a 28 days cycle.	
Reporting group title	Group B - Provera
Reporting group description:	
Medroxyprogesterone Acetate, Provera, oral, 10 mg/24 hours from days 16-26/cycle.	

Primary: The mean changes in the vascular elasticity.

End point title	The mean changes in the vascular elasticity.[1]
End point description:	
End point type	Primary
End point timeframe:	
Changes in vascular elasticity between baseline and visit 5	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no statistical difference seen between the 2 treatment arms for the primary endpoint. Please see attached report for other endpoint analysis.

End point values	Group A - Utrogestan	Group B - Provera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: Change in vascular elasticity	34	34		

Attachments (see zip file)	FINAL STUDY REPORT/Clinical Study Report POF01 Final

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From first dose of IMP until 30 days post last dose of IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Group A - Utrogestan
Reporting group description: -	
Reporting group title	Group B - Provera
Reporting group description: -	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: As this was a low risk trial accepted through the notification scheme as being as no greater risk than standard of care, no AEs were recorded. Only symptoms were recorded patient completed questionnaires.

Serious adverse events	Group A - Utrogestan	Group B - Provera	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (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			
Shingles			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group A - Utrogestan	Group B - Provera	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24072634