Clinical trial results:
PREOPERATIVE LOCALLY APPLIED OESTROGEN IN POSTMENOPAUSAL WOMEN WITH PELVIC ORGAN PROLAPSE: CHANGES IN SUBJECTIVE AND OBJECTIVE OUTCOME: A PROSPECTIVE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Summary

EudraCT number	2016-000410-30
Trial protocol	AT
Global end of trial date	27 August 2020

Results information

Result version number	v1 (current)
This version publication date	23 September 2021
First version publication date	23 September 2021

Trial information

Trial identification

Sponsor protocol code	EstrogenPOP2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Währinger Gürtel 18-20, Vienna, Austria,
Public contact	Urogynecological Department, Medical University of Vienna, Department of Obstetrics and Gynecology, 0043 140400 29620,
Scientific contact	Urogynecological Department, Medical University of Vienna, Department of Obstetrics and Gynecology, 0043 140400 29620,

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 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2020
Global end of trial reached?	Yes
Global end of trial date	27 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective
- To demonstrate treatment efficacy of preoperative vaginally administered oestrogen in postmenopausal women with symptomatic pelvic organ prolapse in comparison to placebo, measured by a subjective questionnaire

Protection of trial subjects:

The study intervention of applying vaginal cream is not associated with pain or distress.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2016
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	Austria: 103
Worldwide total number of subjects	103
EEA total number of subjects	103

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)	63

From 65 to 84 years	38
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment took place over a 31-month period between January 2017 and August 2020 in two urogynaecology centers in east Austria (Medical University of Vienna and University Hospital Tulln). One hundred and twenty women were randomised to receive either vaginal estrogen cream (n =60) or placebo cream (n=60). Once the target sample size was reached,

Pre-assignment

Screening details:

All eligible patients were referred by a gynecologist and seen by an urogynecologist at the study centers. 176 women were assessed for eligibility.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Estrogen

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Linoladiol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Vaginal use

Dosage and administration details:

The active ingredient of Linoladiol® Estradiol-Emulsion is 0.10mg estradiol in 1g cream and is chemically and biologically identical to endogenous human estradiol.
Women were instructed to use the cream (estrogen as well as placebo) intravaginally with the enclosed applicator once daily for one week, every 48 hours for the following week, and then twice weekly for the remaining 4 weeks (=total treatment duration 6 weeks).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Vaginal use

Dosage and administration details:

The placebo cream contained cetyl alcohol, probylene glycol, triglycerides, hostacerin T3, polysorbate, almond oil, benzyl alcohol and purified water.
Women were instructed to use the cream (estrogen as well as placebo) intravaginally with the enclosed applicator once daily for one week, every 48 hours for the following week, and then twice weekly for the remaining 4 weeks (=total treatment duration 6 weeks).

Number of subjects in period 1	Estrogen	Placebo
Started	51	52
Completed	51	52

Baseline characteristics

Reporting groups	
Reporting group title	Estrogen
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Estrogen	Placebo	Total
Number of subjects	51	52	103
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			
Data are mean ± SD or n (%)			
Units: years			
arithmetic mean	64.3	61.8	
standard deviation	± 9.7	± 10.1	-
Gender categorical			
not applicable - only female			
Units: Subjects			
Female	51	52	103
Male	0	0	0

Subject analysis sets	
Subject analysis set title	estrogen in women with prolapse
Subject analysis set type	Intention-to-treat
Subject analysis set description: 103 of 120 (86%) women provided primary analysis data.	

Reporting group values	estrogen in women with prolapse		
Number of subjects	103		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Data are mean ± SD or n (%)			
Units: years arithmetic mean standard deviation	 62.8 ± 10		
Gender categorical			
not applicable - only female			
Units: Subjects			
Female Male	103 0		

End points

End points reporting groups	
Reporting group title	Estrogen
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	estrogen in women with prolapse
Subject analysis set type	Intention-to-treat
Subject analysis set description: 103 of 120 (86%) women provided primary analysis data.	

Primary: Difference of prolapse domain score and other pelvic floor domain scores baseline minus 6 weeks of estrogen treatment	
End point title	Difference of prolapse domain score and other pelvic floor domain scores baseline minus 6 weeks of estrogen treatment
End point description:	
End point type	Primary
End point timeframe: assessment from January 2017 and August 2020	

End point values	Estrogen	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	52		
Units: score				
number (not applicable)	51	52		

Attachments (see zip file)	Tables BJOG revised.docx

Statistical analyses	
Statistical analysis title	Difference of prolapse domain score and other pelv
Comparison groups	Estrogen v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: January 2017 October 2020	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	1
Reporting groups	
Reporting group title	subjects

Reporting group description: -

Serious adverse events	subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 103 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 103 (0.97%)		
Skin and subcutaneous tissue disorders			
skin intolerance			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported