Clinical trial results:
Prevention of preterm birth in women at risk identified by ultrasound: evaluation of two treatment strategies.

Summary

EudraCT number	2012-000241-13
Trial protocol	ES
Global end of trial date	23 March 2016

Results information

Result version number	v1 (current)
This version publication date	15 March 2022
First version publication date	15 March 2022
Summary attachment (see zip file)	Cervical_Pessary_Compared_With_Vaginal.15.aspx (2018 Cervical_Pessary_Compared_With_Vaginal.97935.pdf)

Trial information

Trial identification

Sponsor protocol code	PESAPRO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01643980
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hospital Universitario Puerta de Hierro Majadahonda
Sponsor organisation address	Clinical Pharmacology, Manuel de Falla 1, Majadahonda, Madrid, Spain, 28222
Public contact	Cristina Avendaño-Solá, Servicio de Farmacologia Clínica, 0034 911916479, farmacologia_clinica@idiphim.org
Scientific contact	Cristina Avendaño-Solá, Servicio de Farmacologia Clínica, 0034 911916479, farmacologia_clinica@idiphim.org

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 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2016
Global end of trial reached?	Yes
Global end of trial date	23 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effectiveness of a cervical pessary and vaginal progesterone to prevent spontaneous preterm births in pregnant women with cervical lengths
25 mm or less as measured by transvaginal ultrasonography

Protection of trial subjects:

Both treatment arms are standard treatments and no additional risk or painful procedures are performed. Enrolled women had access to the clinical investigator in case of intercurrent events. Although a third control arm with placebo would have been very valuable from a methodological point of view in a noninferiority comparative trial, it was discarded by ethical and feasibility reasons, as most participant hospitals were already treating these women with a short cervix (either with a pessary or with progesterone) as a measure to decrease the risk of preterm birth, based on recent publications.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 254
Worldwide total number of subjects	254
EEA total number of subjects	254

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)	254

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participating Obstetrics Units routinely perform transvaginal ultrasonography in the second term as a screening diagnosis method to detect women at risk of
preterm birth. Women identified at that tiem point were offered to participate.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	cervical pessary

Arm description: -

Arm type	medical device

No investigational medicinal product assigned in this arm

Arm title	progesterone

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	progesterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal tablet
Routes of administration	Vaginal use

Dosage and administration details:

200 mg micronized progesterone per day by vaginal route (women self-administered the medicine once daily, preferably before going to bed)

Number of subjects in period 1	cervical pessary	progesterone
Started	128	126
Completed	128	126

Period 2

Period 2 title	overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	cervical pessary

Arm description:

Perforated-cerclage type pessary, a hypoallergenic silicon medical device certified by European Conformity, size 65/25/32 (65 mm lower larger diameter,
25 mm height and 32 mm upper smaller diameter). The pessary is placed and removed by the Obstetrician at the clinic.

Arm type	medical device

No investigational medicinal product assigned in this arm

Arm title	progesterone

Arm description:

vaginal progesterone (200 mg/24 hours)

Arm type	Active comparator
Investigational medicinal product name	progesterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Vaginal tablet
Routes of administration	Vaginal use

Dosage and administration details:

200 mg micronized progesterone per day by vaginal route (women self-administered the medicine once daily, preferably before going to bed)

Number of subjects in period 2	cervical pessary	progesterone
Started	128	126
Completed	127	119
Not completed	1	7
do not receive medication	-	4
pessary was not placed	1	-
Do not comply selection criteria	-	3

Baseline characteristics

Reporting groups

Reporting group title	baseline

Reporting group description: -

Reporting group values	baseline	Total	
Number of subjects	254	254	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	254	254	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	254	254	
Male	0	0	

Subject analysis sets

Subject analysis set title	Per protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol subset will be used to test the noninferiority hypothesis.

Reporting group values	Per protocol		
Number of subjects	243		
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)	243		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	243		
Male	0		

End points

End points reporting groups

Reporting group title	cervical pessary
Reporting group description: -	
Reporting group title	progesterone
Reporting group description: -	
Reporting group title	cervical pessary
Reporting group description:	
Perforated-cerclage type pessary, a hypoallergenic silicon medical device certified by European Conformity, size 65/25/32 (65 mm lower larger diameter, 25 mm height and 32 mm upper smaller diameter). The pessary is placed and removed by the Obstetrician at the clinic.	
Reporting group title	progesterone
Reporting group description:	
vaginal progesterone (200 mg/24 hours)	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
The per-protocol subset will be used to test the noninferiority hypothesis.	

Primary: spontaneous preterm delivery before 34 weeks of gestation

End point title	spontaneous preterm delivery before 34 weeks of gestation[1]
End point description:	
End point type	Primary
End point timeframe:	
34 weeks gestation	

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: I cannot include the right numbers in the system. Please, see the attached published paper for the statistical analysis

End point values	cervical pessary	progesterone	Per protocol	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	125	118	243	
Units: number of women	18	17	35	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: All women followed until delivery	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Frequency threshold for reporting non-serious adverse events: 5 %

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: Difficult to include the right numbers in the system. Please, see the attached published paper for adverse events reporting

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/30204689