Clinical trial results:
Prostaglandin insert (Propess) versus tran-scervical balloon catheter for out-patient labour induction: A randomised controlled trial of feasibility (PROBIT-F)

Summary

EudraCT number	2017-001914-27
Trial protocol	GB
Global end of trial date	31 March 2019

Results information

Result version number	v1 (current)
This version publication date	06 February 2020
First version publication date	06 February 2020
Summary attachment (see zip file)	Protocol V3.0 (PROBIT Protocol v3.0.pdf) Final Report (212856_Probit-F_Final_Report V1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	13.0029

Additional study identifiers

ISRCTN number	ISRCTN03199820
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	St George’s Joint Research and Enterprise Services (JRES)
Sponsor organisation address	Jenner Wing, Ground Floor, Cranmer Terrace, London, United Kingdom, SW17 0RE
Public contact	St George’s Joint Research and Enterprise Services (JRES), St George’s Joint Research and Enterprise Services (JRES), 0044 20 8266 6397, sponsor@sgul.ac.uk
Scientific contact	St George’s Joint Research and Enterprise Services (JRES), St George’s Joint Research and Enterprise Services (JRES), 0044 20 8266 6397, sponsor@sgul.ac.uk

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	29 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2019
Global end of trial reached?	Yes
Global end of trial date	31 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a feasibility study. The primary objective is to determine the feasibility of conducting a randomised controlled trial of Prostaglandin pessary versus trans-cervical balloon catheter for out-patient induction of labour.

Protection of trial subjects:

The current study has shown that the options of induction of labour in the out-patient setting, and the use of mechanical methods for labour induction are acceptable to women. However, the current criteria for eligibility for out-patient IOL are restrictive, so that only a small minority of women undergoing IOL are found suitable for out-patient induction. The qualitative data from the current study shows that women were positive about CRB because it did not involve hormones and appeared a more gentle first IOL intervention. The vast majority of participants felt that going home would be beneficial to them.
A previously published study has shown that for women with an unfavourable cervix at term, success of induction of labour with a mechanical method is similar to induction of labour with progstaglandins, with fewer maternal and neonatal side-effects, but similar Caesarean section rates (Jozwiac, 2011). Pain scores are known to be lower in women using mechanical methods of labour induction in the in-patient setting (Pennell et al, 2009). The present study was not powered to explore differences in clinical outcomes, nor the safety of out-patient IoL. The intended sample size could not be reached due to restrictive local guidelines for out-patient induction of labour. The restrictions were made due to safety concerns about outpatient induction. To overcome this and provide the necessary safety data, a large observational study is necessary. Members of the current study team have been successful in securing funding for such an observational study (CHOICE study, NIHR127569). It is possible to make criteria for suitability of out-patient IoL more permissive if the safety of out-patient IoL is demonstrated with an observational study.
Comparison of clinical outcomes from outpatient with inpatient CRB treatment for low risk labour induction would be a useful study to assess the effect of the setting of IoL (out-patient versus in-patient).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2017
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	United Kingdom: 84
Worldwide total number of subjects	84
EEA total number of subjects	84

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

Subject disposition

Recruitment

Recruitment details:

Open to recruitment: 22/09/2017
Recruitment end date (Actual): 31/01/2019

Pre-assignment

Screening details:

Inclusion: Pregnant women aged 18 years or over with a single fetus and uncomplicated pregnancy, who were at a Gestational age > 37 completed weeks, needing induction of labour.
Exclusion: Unsuitable for outpatient management; Unsuitable for randomisation to either and pre-medical health conditions that condition safety

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervical Ripening Balloon catheter

Arm description:

The second is a catheter - a soft rubber tube with an inflatable balloon at the tip. The balloon is placed in the cervix causing it to soften and release natural hormones (prostaglandins) produced by the woman's body.

Arm type	Experimental
Investigational medicinal product name	Cervocal Ripening Balloon with Stylet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Vaginal use

Dosage and administration details:

The Cook Cervical Ripening Balloon is a silicone double-balloon catheter with an adjustable-length malleable stylet.

Arm title	Propess

Arm description:

The method uses dinoprostone, a synthetic hormone administered as a pessary (Propess) introduced in the vagina that delivers prostaglandin over 24 hours

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

Dosage and administration details:

PROPESS 10mg vaginal delivery system

Number of subjects in period 1[1]	Cervical Ripening Balloon catheter	Propess
Started	18	20
Completed	12	17
Not completed	6	3
Consent withdrawn by subject	1	1
IoL not started	1	2
Lack of efficacy	4	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Please, see the attached Final Study Report

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description:

The rate of induction of labour (IoL) has increased steadily over the last decade. Out-patient IoL is considered feasible but there is insufficient evidence about women's preference, or which intervention is the most effective and safe to use in outpatient settings.
An open-label feasibility RCT was conducted in two UK maternity units from October 2017 to March 2019.

Reporting group values	Overall trial	Total	
Number of subjects	38	38	
Age categorical			
Participant characteristics at randomisation – The women had a mean height of 168.9 cm, mean weight 69.1 Kg, and mean BMI 24.2 kg/m2. 25/38 (65.8%) women were nulliparous. The majority of women (29, 76%) were of white European ethnicity. The mean age of women in the dinoprostone group was 34.1 years, compared to 33.2 years in the CRB group.			
Units: Subjects			
Adults (18-64 years)	76	38	
Age continuous			
Participant characteristics at randomisation – The women had a mean height of 168.9 cm, mean weight 69.1 Kg, and mean BMI 24.2 kg/m2. 25/38 (65.8%) women were nulliparous. The majority of women (29, 76%) were of white European ethnicity. The mean age of women in the dinoprostone group was 34.1 years, compared to 33.2 years in the CRB group. T			
Units: years			
arithmetic mean	34.1		
full range (min-max)	18 to 64	-	
Gender categorical			
Female			
Units: Subjects			
Female	38	38	

End points

End points reporting groups

Reporting group title	Cervical Ripening Balloon catheter

Reporting group description:

The second is a catheter - a soft rubber tube with an inflatable balloon at the tip. The balloon is placed in the cervix causing it to soften and release natural hormones (prostaglandins) produced by the woman's body.

Reporting group title	Propess

Reporting group description:

The method uses dinoprostone, a synthetic hormone administered as a pessary (Propess) introduced in the vagina that delivers prostaglandin over 24 hours

Primary: Last data entry point.

End point title	Last data entry point.[1]

End point description:

End point type	Primary

End point timeframe:

End of the study is defined as the last data entry point. (as describe on the Protocol)

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: Please, see the attached Final Study Report

End point values	Cervical Ripening Balloon catheter	Propess		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Decimal Number	18	20		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: since the first recruited participants until the last day of follow up for the last recruited participant.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	DAIDS
Dictionary version	unk

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: Please, see the attached Final Study Report

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2017	SAM01_AM02 Adverts to promote study awareness to staff and potential participants
10 January 2018	SAM02_AM04 Eligibility criteria refined to reflect hospital policy for IOL and detail added regarding qualitative study to include audio recording of study invitation and clarity added over inclusion of birth partner to capture their experience
25 June 2018	SAM03_AM05 Change of study personnel – Sponsor Representative, TMG & TSC members. Clarification on when potential participants can be provided study information. Addition of Midwife interviews. Addition of audio-recording of discussions/interviews. Minor typographical errors corrected. New Data Protection Act 2018 transparency information added to information sheets

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In total, 84 (36.5%) women gave consent to participate. The remaining 40 women did not decline but did not give consent for various reasons. Overall, 38 of the 84 agreeing women were randomised for participation in the trial.

Notes: