Clinical trial results:
CONDISOX: Continued versus discontinued oxytocin stimulation of labour in a double-blind randomised controlled trial

Summary

EudraCT number	2015-002942-30
Trial protocol	DK NL
Global end of trial date	02 July 2020

Results information

Result version number	v1 (current)
This version publication date	20 May 2021
First version publication date	20 May 2021

Trial information

Trial identification

Sponsor protocol code	01012015

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Obstetrics and Gynecology, Regional Hospital of Randers
Sponsor organisation address	Skovlyvej 15, Randers, Denmark,
Public contact	Regional Hospital of Randers, Department of Obstetrics and Gynecology, Regional Hospital of Randers, sidander@rm.dk
Scientific contact	Regional Hospital of Randers, Department of Obstetrics and Gynecology, Regional Hospital of Randers, sidander@rm.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	22 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2020
Global end of trial reached?	Yes
Global end of trial date	02 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The proposed study will investigate the effect of Syntocinon® to induce labour. The hypothesis to be studied is that once labour is established and the active phase of labour has commenced, Syntocinon® can be discontinued and the labour process will continue. The primary outcome will be the rate of caesarean delivery. The main secondary outcomes will be the duration of labour, neonatal conditions, maternal outcomes and satisfaction

Protection of trial subjects:

Participants received standard care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2016
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	Netherlands: 109
Country: Number of subjects enrolled	Denmark: 1091
Worldwide total number of subjects	1200
EEA total number of subjects	1200

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)	1200
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Women at 37–42 complete weeks of gestation stimulated with oxytocin infusion for induction of labour (with or without cervical priming by prostaglandin or cervical ripening catheter).

Pre-assignment

Screening details:

singleton pregnancy
aged >18 years
cephalic position of the baby

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	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Discontinued

Arm description:

IN the active stage of labour oxytocin infusion will be replaced with intravenous infusion of 1 ml isotonic saline diluted in 1000 ml of isotonic saline (Denmark) or 1 ml isotonic saline diluted in 50 ml of isotonic saline (The Netherlands) and infusion will be continued until delivery.

Arm type	Experimental
Investigational medicinal product name	Oxytocin
Investigational medicinal product code	H 01 BB 02
Other name	Syntocinon
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

An intravenous infusion of 10 IU Syntocinon® diluted in 1000 ml of isotonic saline (Denmark) or 5 IU Syntocinon® diluted in 50 ml of isotonic saline (The Netherlands) was started at 3.3 mIU/minute and increased every 20 min by 3.3 mIU/minute until regular contractions (three to five contractions every 10min) were achieved. The maximal authorized infusion rate was 30 mIU/minute.

Arm title	Continued

Arm description:

In the active stage of labour infusion will be replaced with intravenous infusion of 10 IU Syntocinon® diluted in 1000 ml of isotonic saline (Denmark) or 5 IU Syntocinon® diluted in 50 ml of isotonic saline (The Netherlands) and continued until delivery

Arm type	Routine
Investigational medicinal product name	Oxytocin
Investigational medicinal product code	H 01 BB 02
Other name	Syntocinon
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

An intravenous infusion of 10 IU Syntocinon® diluted in 1000 ml of isotonic saline (Denmark) or 5 IU Syntocinon® diluted in 50 ml of isotonic saline (The Netherlands) was started at 3.3 mIU/minute and increased every 20 min by 3.3 mIU/minute until regular contractions (three to five contractions every 10min) were achieved. The maximal authorized infusion rate was 30 mIU/minute.

Number of subjects in period 1	Discontinued	Continued
Started	607	593
Completed	607	591
Not completed	0	2
Consent withdrawn by subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Discontinued
Reporting group description:	
IN the active stage of labour oxytocin infusion will be replaced with intravenous infusion of 1 ml isotonic saline diluted in 1000 ml of isotonic saline (Denmark) or 1 ml isotonic saline diluted in 50 ml of isotonic saline (The Netherlands) and infusion will be continued until delivery.	
Reporting group title	Continued
Reporting group description:	
In the active stage of labour infusion will be replaced with intravenous infusion of 10 IU Syntocinon® diluted in 1000 ml of isotonic saline (Denmark) or 5 IU Syntocinon® diluted in 50 ml of isotonic saline (The Netherlands) and continued until delivery	

Reporting group values	Discontinued	Continued	Total
Number of subjects	607	593	1200
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			
arithmetic mean	31.0	31.3	
standard deviation	± 4.9	± 4.9	-
Gender categorical Units: Subjects			
Female	607	593	1200
Male	0	0	0
White European Units: Subjects			
Yes	531	510	1041
No	52	51	103
Not recorded	24	32	56
Smoking during pregnancy Units: Subjects			
Yes	96	79	175
No	496	502	998
No reported	15	12	27
Married or living with a partner Units: Subjects			
Yes	538	534	1072
No	59	52	111

Not reported	10	7	17
Parity Units: Subjects			
Nulliparous	404	398	802
Parous with no previous Caesarean section	147	155	302
Parous with previous Caesarean section	56	38	94
Not reported	0	2	2
Indication for labour induction Units: Subjects			
Ruptured membranes	230	221	451
Diabetes	43	39	82
Postdate pregnancy	102	120	222
Hypertensive disorders	66	71	137
BMI>35	24	18	42
Oligehydramnios	14	8	22
Maternal request	27	21	48
Other	101	95	196
Cervical ripening Units: Subjects			
Prostaglandins	253	237	490
Cervical ripening catheter	84	85	169
Both	39	40	79
Not reported	0	2	2
None	231	229	460
Female sex of newborn Units: Subjects			
Yes	283	275	558
No	324	316	640
Not reported	0	2	2
Cervical dilatation at randomisation Units: Subjects			
<6	15	7	22
=6	256	272	528
=7	108	118	226
=8	96	71	167
=9	52	33	85
=10	63	64	127
Not reported	17	28	45
Pre-pregnancy BMI Units: kg/m2			
median	25.2	24.8	
inter-quartile range (Q1-Q3)	22.2 to 29.8	22.1 to 29.0	-
Length. of gestation at birth Units: full weeks + days			
median	40.43	40.43	
inter-quartile range (Q1-Q3)	39.14 to 41.29	39.14 to 41.43	-
Birthweight Units: grams			
arithmetic mean	3646	3596	
standard deviation	± 509	± 502	-

End points

End points reporting groups

Reporting group title	Discontinued
Reporting group description:	
IN the active stage of labour oxytocin infusion will be replaced with intravenous infusion of 1 ml isotonic saline diluted in 1000 ml of isotonic saline (Denmark) or 1 ml isotonic saline diluted in 50 ml of isotonic saline (The Netherlands) and infusion will be continued until delivery.	
Reporting group title	Continued
Reporting group description:	
In the active stage of labour infusion will be replaced with intravenous infusion of 10 IU Syntocinon® diluted in 1000 ml of isotonic saline (Denmark) or 5 IU Syntocinon® diluted in 50 ml of isotonic saline (The Netherlands) and continued until delivery	

Primary: Mode of delivery

End point title	Mode of delivery
End point description:	
End point type	Primary
End point timeframe:	
At delivery	

End point values	Discontinued	Continued		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	607	591		
Units: subjects				
Caesarean section	101	84		
Instrumental delivery	64	67		
Vaginal delivery	442	440		

Statistical analyses

Statistical analysis title	Primary outcome - relative risk
Comparison groups	Discontinued v Continued
Number of subjects included in analysis	1198
Analysis specification	Pre-specified
Analysis type	superiority
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.53

Secondary: Indication for Caesarean section

End point title	Indication for Caesarean section

End point description:

End point type	Secondary

End point timeframe:
at delivery

End point values	Discontinued	Continued		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	84		
Units: subjects				
Dystocia	62	58		
Suspicion of fetal asphyxia	26	13		
Suspicion of uterine rupture	3	1		
CHorioamnionitis	2	1		
Other	8	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration from start of initial oxytocin infusion to delivery

End point title	Duration from start of initial oxytocin infusion to delivery

End point description:

End point type	Secondary

End point timeframe:
At delivery

End point values	Discontinued	Continued		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	607	591		
Units: minutes				
median (inter-quartile range (Q1-Q3))	535 (314 to 797)	477 (272 to 727)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration from time of randomisation to delivery

End point title	Duration from time of randomisation to delivery

End point description:

End point type	Secondary

End point timeframe:

At delivery

End point values	Discontinued	Continued		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	607	591		
Units: minutes				
median (inter-quartile range (Q1-Q3))	282 (119 to 484)	203 (77 to 397)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of second stage of labour

End point title	Duration of second stage of labour

End point description:

End point type	Secondary

End point timeframe:

At delivery

End point values	Discontinued	Continued		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	607	591		
Units: minutes				
median (inter-quartile range (Q1-Q3))	95 (31 to 198)	78 (29 to 182)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Until 7 days postpartum	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	Summary of Products
Dictionary version	latest
Reporting groups	
Reporting group title	Continued
Reporting group description: Randomised to continuous stimulation	
Reporting group title	discontinued
Reporting group description: Randomised to discontinued treatment	

Serious adverse events	Continued	discontinued	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 591 (0.00%)	1 / 607 (0.16%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Perinatal death			
subjects affected / exposed	0 / 591 (0.00%)	1 / 607 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Continued	discontinued	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	300 / 591 (50.76%)	300 / 607 (49.42%)	
Pregnancy, puerperium and perinatal conditions			
Postpartumhaemorhage >500 mL			
subjects affected / exposed	259 / 591 (43.82%)	243 / 607 (40.03%)	
occurrences (all)	259	243	
Retained products of conception			

subjects affected / exposed	45 / 591 (7.61%)	39 / 607 (6.43%)	
occurrences (all)	45	39	
3rd and 4th degree perineal tear			
subjects affected / exposed	27 / 591 (4.57%)	25 / 607 (4.12%)	
occurrences (all)	27	25	
Urineretention			
subjects affected / exposed	20 / 591 (3.38%)	25 / 607 (4.12%)	
occurrences (all)	20	25	
Umbilical cord blood pH <7.1			
subjects affected / exposed	40 / 591 (6.77%)	42 / 607 (6.92%)	
occurrences (all)	40	42	
Apgar score <7 at 5 minutes			
subjects affected / exposed	6 / 591 (1.02%)	4 / 607 (0.66%)	
occurrences (all)	6	4	

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/30125998