Clinical trial results:
Ropivacaine Perineal Infiltration for Postpartum Pain Management in Episiotomy Repair: a Double-blind, Randomised, Placebo-controlled Trial

Summary

EudraCT number	2016-002786-62
Trial protocol	FR
Global end of trial date	04 November 2020

Results information

Result version number	v1 (current)
This version publication date	03 September 2022
First version publication date	03 September 2022

Trial information

Trial identification

Sponsor protocol code	CHD065-16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03084549
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Hospitalier Départemental Vendée
Sponsor organisation address	Bd Stephane MOREAU, La Roche sur Yon, France, 85925
Public contact	Dorion Agnès, Centre Hospitalier Départemental Vendée, +33 251446380, agnes.dorion@ght85.fr
Scientific contact	Dr Guillaume DUCARME, Centre Hospitalier Départemental Vendée, guillaume.ducarme@ght85.fr

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	24 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 May 2020
Global end of trial reached?	Yes
Global end of trial date	04 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary outcome was the rate of perineal pain, defined by a Numerical Pain Rating Scale (NPRS) exceeding 3/10, in the mid-term (day 7) postpartum period.

Protection of trial subjects:

All adverse events or reactions (except those specified in the protocol), whether expected or unexpected, serious or not, were collected in the eCRF.
The follow-up of events or adverse reactions, serious or not, was ensured until resolution or consolidation

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 272
Worldwide total number of subjects	272
EEA total number of subjects	272

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)	272

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Inclusion period: 36 months
First inclusion: 2017/20/24
Last inclusion: 2020/04/29

Pre-assignment

Screening details:

Women who had given birth to a singleton foetus in cephalic presentation at 37 weeks of gestation or more, with spontaneous or operative vaginal delivery under epidural anaesthesia and who had received mediolateral episiotomy were eligible for enrolment in the study.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ropivacaine

Arm description:

Eligible women were receive 75 mg of ropivacaine (Fresenius Kabi) in a 20-mL syringe (10-mL of ropivacaine 7.5mg/mL and 10-mL of normal saline)

Arm type	Experimental
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	N01BB09
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

syringe with 10-mL of ropivacaine 7.5mg/mL and 10-mL of normal saline
One injection

Arm title	Placebo

Arm description:

20 mL of normal saline

Arm type	Placebo
Investigational medicinal product name	Chlorure de sodium
Investigational medicinal product code	B05XA03
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

20 mL
one injection

Number of subjects in period 1	Ropivacaine	Placebo
Started	135	137
immediate postpartum period H12,H24,H48	135	137
day 7 postpartum	135	137
long-term postpartum M3	135	137
long-term postpartum M6	135	137
Completed	135	137

Baseline characteristics

Reporting groups	
Reporting group title	Ropivacaine
Reporting group description:	
Eligible women were receive 75 mg of ropivacaine (Fresenius Kabi) in a 20-mL syringe (10-mL of ropivacaine 7.5mg/mL and 10-mL of normal saline)	
Reporting group title	Placebo
Reporting group description:	
20 mL of normal saline	

Reporting group values	Ropivacaine	Placebo	Total
Number of subjects	135	137	272
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	135	137	272
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	30.0	30.3	
standard deviation	± 4.5	± 4.6	-
Gender categorical			
Units: Subjects			
Female	135	137	272
Male	0	0	0

End points

End points reporting groups

Reporting group title	Ropivacaine
Reporting group description:	
Eligible women were receive 75 mg of ropivacaine (Fresenius Kabi) in a 20-mL syringe (10-mL of ropivacaine 7.5mg/mL and 10-mL of normal saline)	
Reporting group title	Placebo
Reporting group description:	
20 mL of normal saline	

Primary: Perineal pain

End point title	Perineal pain
End point description:	
The primary outcome was the analgesic efficacy of ropivacaine at day 7 postpartum (medium term) measured with the numerical pain rating scale (NPRS), exceeding 3/10 in the perineal repair area	
End point type	Primary
End point timeframe:	
day 7 postpartum	

End point values	Ropivacaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	115		
Units: number	39	35		

Statistical analyses

Statistical analysis title	Perineal Pain
Comparison groups	Ropivacaine v Placebo
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Regression, Linear

Adverse events

Adverse events information

Timeframe for reporting adverse events:

data were collected from randomisation to the immediate postpartum period at H48

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Ropivacaine
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Ropivacaine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 135 (2.22%)	4 / 137 (2.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Incorrect route of product administration			
subjects affected / exposed	0 / 135 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haemorrhage			
subjects affected / exposed	0 / 135 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Perineal haematoma			
subjects affected / exposed	1 / 135 (0.74%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum haemorrhage			

subjects affected / exposed	0 / 135 (0.00%)	2 / 137 (1.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Lactation disorder			
subjects affected / exposed	1 / 135 (0.74%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 135 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Genital abscess			
subjects affected / exposed	1 / 135 (0.74%)	0 / 137 (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: 5 %

Non-serious adverse events	Ropivacaine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 135 (85.93%)	129 / 137 (94.16%)	
Injury, poisoning and procedural complications			
Incision site haematoma			
subjects affected / exposed	4 / 135 (2.96%)	1 / 137 (0.73%)	
occurrences (all)	4	1	
Incision site haemorrhage			
subjects affected / exposed	1 / 135 (0.74%)	1 / 137 (0.73%)	
occurrences (all)	1	1	
Incision site pain			
subjects affected / exposed	97 / 135 (71.85%)	107 / 137 (78.10%)	
occurrences (all)	129	135	
Postoperative wound complication			

subjects affected / exposed	3 / 135 (2.22%)	1 / 137 (0.73%)	
occurrences (all)	3	1	
Suture related complication			
subjects affected / exposed	2 / 135 (1.48%)	1 / 137 (0.73%)	
occurrences (all)	2	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	21 / 135 (15.56%)	15 / 137 (10.95%)	
occurrences (all)	21	15	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 135 (0.74%)	3 / 137 (2.19%)	
occurrences (all)	1	3	
Pregnancy, puerperium and perinatal conditions			
Perineal haematoma			
subjects affected / exposed	8 / 135 (5.93%)	14 / 137 (10.22%)	
occurrences (all)	8	14	
Postpartum haemorrhage			
subjects affected / exposed	15 / 135 (11.11%)	17 / 137 (12.41%)	
occurrences (all)	15	17	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 135 (4.44%)	6 / 137 (4.38%)	
occurrences (all)	6	6	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	8 / 135 (5.93%)	11 / 137 (8.03%)	
occurrences (all)	9	12	
Pyrexia			
subjects affected / exposed	2 / 135 (1.48%)	1 / 137 (0.73%)	
occurrences (all)	2	1	
Oedema			
subjects affected / exposed	7 / 135 (5.19%)	7 / 137 (5.11%)	
occurrences (all)	7	7	
Reproductive system and breast disorders			

Oedema genital			
subjects affected / exposed	3 / 135 (2.22%)	8 / 137 (5.84%)	
occurrences (all)	3	8	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 135 (0.74%)	4 / 137 (2.92%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Coccydynia			
subjects affected / exposed	0 / 135 (0.00%)	2 / 137 (1.46%)	
occurrences (all)	0	2	
Infections and infestations			
Amniotic cavity infection			
subjects affected / exposed	1 / 135 (0.74%)	1 / 137 (0.73%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	2 / 135 (1.48%)	1 / 137 (0.73%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2017	Modification of the dose and administered concentration of Ropivacaine
21 March 2018	Modification of the labelling of the treatment boxes
12 September 2018	Modification of AE notification procedure updated consent form (implementation of REGULATION (EU) 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL)
26 March 2019	extension of study period (+18 months)
02 March 2020	update Ropivacaine's Summary of Product Characteristics

Notes:

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/35876236