Clinical trial results:
Programmed Intermittent Epidural Bolus versus Continuous Epidural Infusion for third trimester voluntary termination of pregnancy analgesia : a randomized study.

Summary

EudraCT number	2015-001738-33
Trial protocol	FR
Global end of trial date	11 December 2018

Results information

Result version number	v1 (current)
This version publication date	05 June 2021
First version publication date	05 June 2021
Summary attachment (see zip file)	RRF PCEA IMG (RRF PCEA final.pdf) statistical report (Rapport d'analyse statistique et de sécurité PCEA-IMG V1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	I14032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02744482
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de LIMOGES
Sponsor organisation address	2 Avenue Martin Luther King -, Limoges, France, 87042
Public contact	Director Recherche and Innovation, CHU de LIMOGES, +33 555056349, drc@chu-limoges.fr
Scientific contact	Principal investigator, CHU de LIMOGES, +33 555052103, patrick.senges@chu-limoges.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	21 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2018
Global end of trial reached?	Yes
Global end of trial date	11 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate the benefit PIEB mode compared with the standard mode CEI in the Voluntary termination of pregancy after 22 weeks in terms of satisfaction with analgesia.

Protection of trial subjects:

no particular protection

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
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	France: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	37
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

no pre-assignment period

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	PCEA-BIP

Arm description: -

Arm type	Experimental
Investigational medicinal product name	levobupivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use

Dosage and administration details:

Maximum of 342,92 mg per day in mix with Sufentanil citrate and clonidine for epidural use

Investigational medicinal product name	Sufentanil citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use

Dosage and administration details:

Maximum of 189,45 µg per day in mix with levobupivacaine and clonidine for epidural use

Investigational medicinal product name	Clonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use

Dosage and administration details:

Maximum of 669,3 µg per day in mix with levobupivacaine and sufentanil citrate for epidural use

Arm title	PCEA-DC

Arm description:

-Injection of a 2 mL initial epidural loading dose consisting of a blend of 8 mL of levobupivacaine 2,5mg/mL plus 2 mL of sufentanil 5 µg/mL to assure the absence of motor block and so exclude intrathecal placement of the epidural catheter.
-Injection of the rest of the loading dose (8mL).
-In this group the pump is programmed to deliver a continuous infusion at 10 mL /h consisting of levobupivacaine 0,573 mg/mL plus sufentanil 0,37 µg/mL plus clonidine 1,38 µg/mL. Additional 5 mL patient-activated boluses will be allowed with a lockout interval of 10 minutes.
-If the parturient feels she has inadequate analgesia after having activated the PCEA bolus twice in a thirty minutes period, an additional manual bolus of 6 mL of levobupivacaine 2,5 mg/mL will be administered until the Pain Visual Analog Scale (PVAS) is < 30/100 with a limit of 3 injections by hour

before that the anesthetist to be called.

Arm type	Active comparator
Investigational medicinal product name	levobupivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use
Dosage and administration details: Maximum of 350,09 mg per day in mix with Sufentanil citrate and clonidine for epidural use	
Investigational medicinal product name	Sufentanil citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use
Dosage and administration details: Maximum of 192,23 µg per day in mix with levobupivacaine and clonidine for epidural use	
Investigational medicinal product name	Clonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Epidural use
Dosage and administration details: Maximum of 685,08 µg per day in mix with levobupivacaine and sufentanil citrate for epidural use	

Number of subjects in period 1	PCEA-BIP	PCEA-DC
Started	18	19
Completed	17	17
Not completed	1	2
intervention not received	1	1
failure of the procedure	-	1

Baseline characteristics

Reporting groups	
Reporting group title	PCEA-BIP
Reporting group description: -	
Reporting group title	PCEA-DC

Reporting group description:

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Reporting group values	PCEA-BIP	PCEA-DC	Total
Number of subjects	18	19	37
Age categorical Units: Subjects			
Adults (18-64 years)	18	19	37
Age continuous Units: years			
median	28.9	30.8	
full range (min-max)	20 to 39	22 to 45	-
Gender categorical Units: Subjects			
Female	18	19	37
Male	0	0	0

End points

End points reporting groups

Reporting group title	PCEA-BIP
Reporting group description: -	
Reporting group title	PCEA-DC

Reporting group description:

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Subject analysis set title	PCEA-BIP
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients included in PCEA-BIP arm and received procedure

Subject analysis set title	PCEA-DC
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients included in PCEA-DC arm and receivded procedure

Primary: Satisfaction visual analog scale (SVAS) measurment

End point title	Satisfaction visual analog scale (SVAS) measurment[1]

End point description:

The degree of satisfaction is assessed using a satisfaction visual analog scale (SVAS) where 0 corresponded to " completely unsatisfied " and 100 to " completely satisfied ".

End point type	Primary

End point timeframe:

end of participation

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: see statistical report joined

End point values	PCEA-BIP	PCEA-DC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	17		
Units: no unit				
number (not applicable)	88.4	85		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: overall trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22
Reporting groups	
Reporting group title	all patients

Reporting group description: -

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Postpartum haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 34 (35.29%)		
Injury, poisoning and procedural complications			
Lateralization of the epidural			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Cardiac disorders			
arterial hypotention			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		

Pregnancy, puerperium and perinatal conditions			
placental retention			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Uterine atony			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2015	- Modification of service practices - Modification of the type of scale taken into account when calculating the number of subjects required - Modification of the nature of the randomization, the nature of the CRF and the correction of the maximum dose per 14h received by the patients depending on the arm
26 December 2017	- Modification RCP catapressan and sufenta - Deletion of the non-inclusion criteria for patients treated with sultopride - Modification of a CNI to add the taking of agniste to the nalmefene
22 March 2018	Prolongation of inclusion period
19 October 2018	prolongation of inclusion period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported