Clinical trial results:
RANDOMIZED AND CONTROLLED PHASE IV CLINICAL TRIAL ON THE ANALGESIC EFFECTIVENESS OF THE COMBINED BLOCKADE (PENG - PERICAPSULAR NERVE GROUP- AND THE FEMORAL LATERAL CUTANEOUS NERVE) IN THE HIP FRACTURES OF THE ELDERLY. COMPARATIVE STUDY BETWEEN LEVOBUPIVACAINE AND ROPIVACAINE.

Summary

EudraCT number	2020-004697-21
Trial protocol	ES
Global end of trial date	01 December 2021

Results information

Result version number	v1 (current)
This version publication date	29 January 2022
First version publication date	29 January 2022

Trial information

Trial identification

Sponsor protocol code	PENG-CAD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fundación IECSCYL-IBSAL.
Sponsor organisation address	Hospital Virgen de la Vega, 10ª Planta. Paseo de San Vicente, 58-182. , Salamanca, Spain, 37007
Public contact	Área de Ensayos Clínicos, SCReN-UICEC CAUSA/IBSAL, +34 9232911005779, ricardo.lopez@scren.es
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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	12 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2021
Global end of trial reached?	Yes
Global end of trial date	01 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the analgesic efficacy of both local anesthetics in the regional block of hip fracture surgery.

Protection of trial subjects:

Adequate information of each patient and efficient monitoring of treatment safety through pharmacovigilance.

Background therapy:

Patients treated with Levobupivacaine Altan 7.5 mg / ml solution for injection and infusion

Evidence for comparator:

Patients treated with Ropivacaine Altan 2 mg / ml solution for infusion

Actual start date of recruitment	09 February 2021
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	Spain: 114
Worldwide total number of subjects	114
EEA total number of subjects	114

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)	0
From 65 to 84 years	41
85 years and over	73

Subject disposition

Recruitment

Recruitment details:

The patient will have to voluntarily sign and understand the informed consent that will be provided in writing

Pre-assignment

Screening details:

Patients over 65 years of age, with a hip fracture, who are going to be operated on at the Salamanca University Assistance Complex (CAUSA), without allergy to any of the drugs,
coagulation disorders, local infections instead of puncture or vascular prostheses at the femoral level.

Period 1

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

Blinding implementation details:

Randomization was carried out using the SPSS © computer program (v. 25.0), generating two treatment groups in a simple random way (1: 1) with allocation in blocks (size 6) of the selected patients included in the study. Two "extra" allocation blocks were generated to assign patients derived from filling in patients withdrawn from the trial (criteria 6.6, PENG-CAD clinical trial protocol, v1 of September 1, 2020).

Arms

Are arms mutually exclusive?	Yes
Arm title	LEVOBUPIVACAINE

Arm description:

Patients treated with Levobupivacaine Altan 7.5 mg / ml solution for injection and infusion

Arm type	Experimental
Investigational medicinal product name	Levobupivacaína Altan 7,5 mg/ml solución inyectable y para perfusión EFG
Investigational medicinal product code	78248
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

0.25 % percent

Arm title	ROPIVACAINE

Arm description:

Patients treated with Ropivacaine Altan 2 mg / ml solution for infusion

Arm type	Active comparator
Investigational medicinal product name	Patients treated with Ropivacaine Altan 2 mg / ml solution for infusion
Investigational medicinal product code	N01BB10
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

0.25 % percent (0.375%)

Number of subjects in period 1	LEVOBUPIVACAINE	ROPIVACAINE
Started	57	57
Completed	56	52
Not completed	1	5
Screening failure	-	1
The patient dies before starting the surgical proc	1	-
Lack of efficacy	-	4

Baseline characteristics

Reporting groups	
Reporting group title	LEVOBUPIVACAINE
Reporting group description:	
Patients treated with Levobupivacaine Altan 7.5 mg / ml solution for injection and infusion	
Reporting group title	ROPIVACAINE
Reporting group description:	
Patients treated with Ropivacaine Altan 2 mg / ml solution for infusion	

Reporting group values	LEVOBUPIVACAINE	ROPIVACAINE	Total
Number of subjects	57	57	114
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			
Patients older than 65 years			
Units: years			
median	86.40	86.13	
standard deviation	± 7.56	± 8.47	-
Gender categorical			
Patients older than 65 years			
Units: Subjects			
Female	41	46	87
Male	16	11	27

Subject analysis sets	
Subject analysis set title	Levobupivacaine
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients treated with Levobupivacaine included in final result	
Subject analysis set title	Ropivacaine
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients treated with Ropivacaine included in final result	

Reporting group values	Levobupivacaine	Ropivacaine	
Number of subjects	56	52	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Patients older than 65 years			
Units: years median standard deviation	 86.11 ± 5.52	 86.69 ± 6.22	
Gender categorical			
Patients older than 65 years			
Units: Subjects			
Female Male	41 15	43 9	

End points

End points reporting groups

Reporting group title	LEVOBUPIVACAINE
Reporting group description: Patients treated with Levobupivacaine Altan 7.5 mg / ml solution for injection and infusion	
Reporting group title	ROPIVACAINE
Reporting group description: Patients treated with Ropivacaine Altan 2 mg / ml solution for infusion	
Subject analysis set title	Levobupivacaine
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients treated with Levobupivacaine included in final result	
Subject analysis set title	Ropivacaine
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients treated with Ropivacaine included in final result	

Primary: Need for rescue drugs

End point title	Need for rescue drugs
End point description: Need for rescue drugs at 6h, 12h, 24h and 48h.	
End point type	Primary
End point timeframe: 6h, 12h, 24h, 48h	

End point values	LEVOBUPIVACAINE	ROPIVACAINE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: number				
6h	10	4		
12h	12	14		
24h	21	17		
48h	10	14		
No rescue	3	3		

Statistical analyses

Statistical analysis title	Rescue
Comparison groups	LEVOBUPIVACAINE v ROPIVACAINE

Number of subjects included in analysis	108
Analysis specification	Post-hoc
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Latency of initiation; EVN

End point title	Latency of initiation; EVN
End point description: Assessed using EVN analgesic scale	
End point type	Secondary
End point timeframe: 6h, 12h, 24h and 48h	

End point values	LEVOBUPIVACAINE	ROPIVACAINE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: point				
median (standard deviation)				
6h	1.92 (± 1.04)	1.68 (± 2.56)		
12h	2.50 (± 2.26)	2.91 (± 3.15)		
24h	4.33 (± 2.79)	3.50 (± 2.82)		
48h	4.72 (± 2.66)	4.58 (± 2.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Latency of initiation; Algoplus

End point title	Latency of initiation; Algoplus
End point description: Assessed using Algoplus analgesic scale	
End point type	Secondary
End point timeframe: 6h, 12h 24h and 48h	

End point values	LEVOBUPIVACAINE	ROPIVACAINE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Point				
median (standard deviation)				
6h	0.94 (± 1.25)	0.75 (± 1.04)		
12h	1.30 (± 1.06)	1.38 (± 1.43)		
24h	2.16 (± 1.37)	1.70 (± 1.28)		
48h	2.32 (± 1.27)	2.21 (± 1.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Latency of initiation; PAINAD

End point title	Latency of initiation; PAINAD
End point description: Assessed using PIANAD analgesic scale	
End point type	Secondary
End point timeframe: 6h, 12h, 24h and 48h	

End point values	LEVOBUPIVACAINE	ROPIVACAINE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Point				
median (standard deviation)				
6h	1.46 (± 2.05)	1.04 (± 1.67)		
12h	1.95 (± 1.69)	1.84 (± 1.99)		
24h	3.22 (± 1.99)	2.76 (± 2.17)		
48h	3.75 (± 2.23)	3.36 (± 2.14)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
At 48 h it is considered the end of follow-up	
Adverse event reporting additional description:	
At 48 h it is considered the end of follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Treated

Reporting group description:

No one serious adverse events were detected.

Serious adverse events	Treated		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 108 (0.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Treated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 108 (0.00%)		

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: No adverse events were detected. Allergic reactions, vascular punctures, nerve injuries, infections and toxicities due to the local anesthetic were evaluated but none were detected.
A serious adverse event was detected. A patient who died of shock before study drugs could be applied. This patient signed the Informed Consent but is not evaluated in the study because he did not receive study treatment.

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

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

The age of the patients often makes it difficult for researchers to interpret pain scales. We did not see differences in the duration or quality of the block between the two anesthetics.

Notes: