Clinical trial results:
Ultrasound-guided Genicular Nerve Block an Analgesic Alternative to LIA for Total Knee Arthroplasty. Randomized clinical trial.

Summary

EudraCT number	2019-005010-19
Trial protocol	ES
Global end of trial date	30 April 2021

Results information

Result version number	v1 (current)
This version publication date	07 September 2022
First version publication date	07 September 2022

Trial information

Trial identification

Sponsor protocol code	HCB/2019/1148

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04681547
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hospital CLÍNIC
Sponsor organisation address	Villaroel 170, Barcelona, Spain, 08036
Public contact	Anestesiología y Reanimación, Hospital Clínic de Barcelona, 34 932275558, cunat@clinic.cat
Scientific contact	Anestesiología y Reanimación, Hospital Clínic de Barcelona, 645152055 932275558, cunat@clinic.cat

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	30 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2021
Global end of trial reached?	Yes
Global end of trial date	30 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to verify that the ultrasound-guided blockade of the genicular nerves is not inferior in terms of analgesic efficacy in comparison with the LIA in the first 24 hours of the postoperative period of primary TKA and during the first mobilization using the NRS score.

Protection of trial subjects:

As the experimental technique was performed as part of the standard care protocol, no additional measures were taken.

Background therapy:

Standard care for TKA

Evidence for comparator:

Ultrasound-guided genicular nerves blockade (GNB) is a technique that has been effectively used for a variety of chronic knee pain conditions and as an analgesic technique in the surgical and acute pain settings selectively targeting sensory branches from the knee capsule.

Actual start date of recruitment	15 December 2020
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	Spain: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	10

From 65 to 84 years	49
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 83 subjects were screened and 60 were enrolled and randomized. One subject in the GNB group was discontinued due to difficulties adhering to study protocol amidst the Covid-19 pandemic. Ultimately, 29 patients in the GNB group and 30 patients in the LIA group were included for analysis.

Pre-assignment

Screening details:

A total of 83 subjects were examined. Finally, 15 refused to participate. Five subjects were excluded because of obesity, 2 because of preference for general anesthesia, and 1 because of excessive baseline opioid use.

Period 1

Period 1 title	Recruitment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Monitor, Data analyst[2]

Blinding implementation details:

Post anaesthesia care unit (PACU) and ward nurses, as well a physical therapists and research assistants, were blinded for treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Local infiltration analgesia

Arm description:

Local infiltration analgesia

Arm type	Active comparator
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	N01BB09
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Solution for injection

Dosage and administration details:

The LIA was performed at the end of the surgical procedure and was based on the administration of ropivacaine 0.2% 150 ml (100 ml of ropivacaine 0.2% with 1 mg of adrenaline during the ischemia period and subsequently, before closure of the surgical wound, 50 ml of ropivacaine 0.2%).

Investigational medicinal product name	Adrenaline
Investigational medicinal product code	C01CA24
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Solution for injection

Dosage and administration details:

Administration of ropivacaine 0.2% 150 ml (100 ml of ropivacaine 0.2% with 1 mg of adrenaline during the period of intraoperative ischemia and, before closure of the surgical wound, 50 ml of ropivacaine 0.2%).

Arm title	Genicular nerves block

Arm description:

Genicular nerves block

Arm type	Experimental

Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	N01BB09
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Solution for injection

Dosage and administration details:

GNB (geniculate nerve block): 4 ml of ropivacaine 0.2%, with adrenaline 1:100 000 was administered in each of the 5 nerves to be blocked (20 ml in total).

Investigational medicinal product name	Adrenaline
Investigational medicinal product code	C01CA24
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Solution for injection

Dosage and administration details:

Four ml of ropivacaine 0.2%, with adrenaline 1:100 000 were administered in each of the 5 nerves to be blocked (20 ml in total).

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: Post anaesthesia care unit (PACU) and ward nurses, as well a physical therapists and research assistants, were blinded for treatment allocation.
[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Post anaesthesia care unit (PACU) and ward nurses, as well a physical therapists and research assistants, were blinded for treatment allocation.

Number of subjects in period 1	Local infiltration analgesia	Genicular nerves block
Started	30	30
Completed	30	29
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Recruitment

Reporting group description: -

Reporting group values	Recruitment	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	10	
From 65-84 years	49	49	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	73		
standard deviation	± 6.62	-	
Gender categorical Units: Subjects			
Female	44	44	
Male	16	16	
ASA Units: Subjects			
ASA I	5	5	
ASA II	41	41	
ASA III	14	14	
Body Mass Index Units: BMI			
arithmetic mean	29.8		
standard deviation	± 4.18	-	
Womac total score Units: Womac			
median			
inter-quartile range (Q1-Q3)		-	
BPI inference Units: BPI			
median			
inter-quartile range (Q1-Q3)		-	
BPI intensity Units: BPI			
median			

inter-quartile range (Q1-Q3)		-	

Subject analysis sets

Subject analysis set title	Overall analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Age, gendre, ASA physical status, BMI, WOMAC score and BPI inference and intensity scores were recorded.

Reporting group values	Overall analysis		
Number of subjects	59		
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)	10		
From 65-84 years	49		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean	72.3		
standard deviation	± 6.66		
Gender categorical			
Units: Subjects			
Female	44		
Male	16		
ASA			
Units: Subjects			
ASA I	5		
ASA II	40		
ASA III	14		
Body Mass Index			
Units: BMI			
arithmetic mean	29.8		
standard deviation	± 4.18		
Womac total score			
Units: Womac			
median	92.5		
inter-quartile range (Q1-Q3)	72.5 to 109		
BPI inference			
Units: BPI			
median	4.7		

inter-quartile range (Q1-Q3)	3.7 to 6		
BPI intensity			
Units: BPI			
median	3.25		
inter-quartile range (Q1-Q3)	2.5 to 5		

End points

End points reporting groups

Reporting group title	Local infiltration analgesia
Reporting group description: Local infiltration analgesia	
Reporting group title	Genicular nerves block
Reporting group description: Genicular nerves block	
Subject analysis set title	Overall analysis
Subject analysis set type	Full analysis
Subject analysis set description: Age, gendre, ASA physical status, BMI, WOMAC score and BPI inference and intensity scores were recorded.	

Primary: 24 h rest NRS

End point title	24 h rest NRS
End point description: 24 h NRS at rest	
End point type	Primary
End point timeframe: 24 h	

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: NRS				
median (inter-quartile range (Q1-Q3))	3 (2.25 to 5)	2 (1 to 3)		

Statistical analyses

Statistical analysis title	24 h NRS at rest
Comparison groups	Genicular nerves block v Local infiltration analgesia
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.025
Method	Wilcoxon (Mann-Whitney)

Secondary: PACU NRS

End point title	PACU NRS

End point description:

End point type	Secondary

End point timeframe:
PACU

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: NRS				
median (inter-quartile range (Q1-Q3))	2 (1 to 4)	2 (0 to 4)		

Statistical analyses

Statistical analysis title	PACU NRS
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.025
Method	Wilcoxon (Mann-Whitney)

Secondary: 12 h NRS

End point title	12 h NRS

End point description:

End point type	Secondary

End point timeframe:
12 h

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: NRS				
median (inter-quartile range (Q1-Q3))	4 (2 to 5)	3 (1 to 5)		

Statistical analyses

Statistical analysis title	12 h NRS
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.025
Method	Wilcoxon (Mann-Whitney)

Secondary: 24 physiotherapy NRS

End point title	24 physiotherapy NRS
End point description:	
End point type	Secondary
End point timeframe:	
24 h	

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: NRS				
median (inter-quartile range (Q1-Q3))	3 (2 to 6)	3 (2 to 4)		

Statistical analyses

Statistical analysis title	24 h physiotherapy NRS
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.025
Method	Wilcoxon (Mann-Whitney)

Secondary: Cumulative OME 24 h consumption

End point title	Cumulative OME 24 h consumption
End point description:	
End point type	Secondary

End point timeframe:
24 h

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: mg				
median (inter-quartile range (Q1-Q3))	5 (0 to 10)	10 (5 to 12)		

Statistical analyses

Statistical analysis title	Cumulative OME 24 h consumption
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.025
Method	Wilcoxon (Mann-Whitney)

Secondary: Minimum articular range

End point title	Minimum articular range

End point description:

End point type	Secondary

End point timeframe:
24 h

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: degrees				
median (inter-quartile range (Q1-Q3))	-2.5 (-5 to 5)	-5 (-5 to 5)		

Statistical analyses

Statistical analysis title	Minimum articular range
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Maximum articular balance	
End point title	Maximum articular balance
End point description:	
End point type	Secondary
End point timeframe:	
24 h	

End point values	Local infiltration analgesia	Genicular nerves block		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: degrees				
median (inter-quartile range (Q1-Q3))	85 (81.3 to 89.5)	85 (80 to 90)		

Statistical analyses

Statistical analysis title	Maximum articular range
Comparison groups	Local infiltration analgesia v Genicular nerves block
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Intra and postoperative period	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
Reporting groups	
Reporting group title	Local infiltration analgesia
Reporting group description: -	
Reporting group title	Genicular nerves block
Reporting group description: -	

Serious adverse events	Local infiltration analgesia	Genicular nerves block	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Local infiltration analgesia	Genicular nerves block	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
Surgical and medical procedures			
Bleeding	Additional description: One patient presented minor postoperative surgical wound bleeding that required transfusion and was treated conservatively.		
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2021	The sample size was modified from 54 to 60 patients (27 to 30 patients per arm). This change was motivated by the need to use unilateral contrast tests in the calculation of the sample size (and therefore with an alpha error of 0.025) when the primary objective is noninferiority and taking into account a dropout of 10%.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported