Clinical trial results:
Ultrasound-guided nerve block of the anterior femoral cutaneous nerves in healthy volunteers

Summary

EudraCT number	2018-004986-15
Trial protocol	DK
Global end of trial date	07 April 2019

Results information

Result version number	v1 (current)
This version publication date	13 November 2019
First version publication date	13 November 2019

Trial information

Trial identification

Sponsor protocol code	Protocol_AFCN_17022019

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle-Juul Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Siska Bjørn , Aarhus University Hospital, +45 60651087, siska.bjoern@post.au.dk
Scientific contact	Thomas Fichtner Bendtsen , Aarhus University Hospital, +45 51542997, tfb@dadlnet.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	31 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 April 2019
Global end of trial reached?	Yes
Global end of trial date	07 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this volunteer trial was to investigate the success of cutaneous anesthesia of the surgical incision for total knee arthroplasty (TKA) when adding a block of the intermediate femoral cutaneous nerve (IFCN) to a proximal femoral triangle block (FTB). Our primary hypothesis was that proximal FTB combined with IFCNB would provide superior cutaneous anesthesia of the surgical incision line compared to proximal FTB alone.

Protection of trial subjects:

This volunteer trial was conducted in accordance with the Declaration of Helsinki and approved by the Danish Medicines Agency (2019023631), The Central Denmark Region Committees on Health Research Ethics (1-10-72-366-18) and the Danish Data Protection Agency. The trial was prospectively registered in the EudraCT database (2018-004986-15) and was monitored by the Good Clinical Practice Unit at Aalborg and Aarhus University Hospitals. Prior to inclusion, written informed consent was obtained from all subjects after a thorough oral and written participant information had been given.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2019
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	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers of 18 years or older were recruited through a Danish website dedicated to recruit volunteers for research (www.forsøgsperson.dk). All volunteers received payment for their participation.

Pre-assignment

Screening details:

Inclusion criteria: > 18 years, ASA score I-II. Exclusion criteria: inability to cooperate/communicate in Danish, weight <60 kg, BMI > 28 kg/m2, lower limb neuropathy, chronic opioid-requiring pain, infection in the areas of injection, pregnancy, allergy to local anesthetic and daily consumption of medicine apart from oral contraceptives.

Period 1

Period 1 title	overall period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomization group 1

Arm description:

Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine).
Leg leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline).

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

Dosage and administration details:

Each volunteer received a total of 40 ml ropivacaine 5 mg/ml = 200 mg ropivacaine during the entire trial period (5-6 hours)

Investigational medicinal product name	Sodium chloride 0.9 %
Investigational medicinal product code	
Other name	Normal saline
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Each volunteer received a total of 40 ml normal saline during the entire trial period (5-6 hours)

Arm title	Randomization group 2

Arm description:

Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline).
Left leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine).

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

Dosage and administration details:

Each volunteer received a total of 40 ml ropivacaine 5 mg/ml = 200 mg ropivacaine during the entire trial period (5-6 hours)

Investigational medicinal product name	Sodium chloride 0.9 %
Investigational medicinal product code	
Other name	Normal saline
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Each volunteer received a total of 40 ml normal saline during the entire trial period (5-6 hours)

Arm title	Randomization group 3

Arm description:

Right leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine)
Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline)

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

Dosage and administration details:

Each volunteer received a total of 40 ml ropivacaine 5 mg/ml = 200 mg ropivacaine during the entire trial period (5-6 hours)

Investigational medicinal product name	Sodium chloride 0.9 %
Investigational medicinal product code	
Other name	Normal saline
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Each volunteer received a total of 40 ml normal saline during the entire trial period (5-6 hours)

Arm title	Randomization group 4

Arm description:

Right leg: PLACEBO distal FTB (20 ml saline) +ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline)
Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine)

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

Dosage and administration details:

Each volunteer received a total of 40 ml ropivacaine 5 mg/ml = 200 mg ropivacaine during the entire trial period (5-6 hours)

Investigational medicinal product name	Sodium chloride 0.9 %
Investigational medicinal product code	
Other name	Normal saline
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Each volunteer received a total of 40 ml normal saline during the entire trial period (5-6 hours)

Number of subjects in period 1	Randomization group 1	Randomization group 2	Randomization group 3
Started	10	10	10
Completed	10	10	10

Number of subjects in period 1	Randomization group 4
Started	10
Completed	10

Baseline characteristics

Reporting groups	
Reporting group title	overall period

Reporting group description: -

Reporting group values	overall period	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
Adults (18-64 years)	40	40	
Age continuous Units: years arithmetic mean standard deviation	 27 ± 6.9	 -	
Gender categorical Units: Subjects			
Female	15	15	
Male	25	25	
ASA score Units: Subjects			
ASA I	40	40	
ASA II	0	0	
BMI			
Body mass index			
Units: kilogram(s)/square meter arithmetic mean standard deviation	 23 ± 1.9	 -	

End points

End points reporting groups

Reporting group title	Randomization group 1
Reporting group description:	
Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine). Leg leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline).	

Reporting group title	Randomization group 2
Reporting group description:	
Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline). Left leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine).	

Reporting group title	Randomization group 3
Reporting group description:	
Right leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine) Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline)	

Reporting group title	Randomization group 4
Reporting group description:	
Right leg: PLACEBO distal FTB (20 ml saline) +ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline) Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine)	

Subject analysis set title	Active proximal FTB + active IFCNB
Subject analysis set type	Per protocol
Subject analysis set description:	
Active proximal FTB + active IFCNB = randomization group 2 + 3	
Subject analysis set title	Active proximal FTB + placebo IFCNB
Subject analysis set type	Per protocol
Subject analysis set description:	
Active proximal FTB + placebo IFCNB = randomization group 1 + 4	
Subject analysis set title	Active distal FTB + active IFCNB
Subject analysis set type	Per protocol
Subject analysis set description:	
Active distal FTB + active IFCNB = randomization groups 1 + 4	
Subject analysis set title	Active distal FTB + placebo IFCNB
Subject analysis set type	Per protocol
Subject analysis set description:	
Active dital FTB + placebo IFCNB = randomization groups 2 + 3	
Subject analysis set title	Active proximal FTB (before IFCNB)
Subject analysis set type	Per protocol
Subject analysis set description:	
Active proximal FTB. Data collection after the first block session before addition of the IFCNB (second block session)	

Subject analysis set title	Active distal FTB (before IFCNB)
Subject analysis set type	Per protocol

Subject analysis set description:

Active distal FTB. Data collection after the first block session before addition of the IFCNB (second block session)

Subject analysis set title	IFCNB right side
Subject analysis set type	Per protocol

Subject analysis set description:

IFCNB performed on the right side

Subject analysis set title	IFCNB left side
Subject analysis set type	Per protocol

Subject analysis set description:

IFCNB performed on the left side

Subject analysis set title	Proximal FTB right side
Subject analysis set type	Per protocol

Subject analysis set description:

Proximal FTB performed on the right side

Subject analysis set title	Proximal FTB left side
Subject analysis set type	Per protocol

Subject analysis set description:

Proximal FTB performed on the left side

Subject analysis set title	Distal FTB right side
Subject analysis set type	Per protocol

Subject analysis set description:

Distal FTB performed on the right side

Subject analysis set title	Distal FTB left side
Subject analysis set type	Per protocol

Subject analysis set description:

Distal FTB performed on the left side

Subject analysis set title	IFCNB right + left side
Subject analysis set type	Per protocol

Subject analysis set description:

Each volunteer had IFCNB bilaterally. For the discomfort the volunteer was asked to give one total score for the discomfort during the IFCNB performance.

Subject analysis set title	Proximal FTB right + left side
Subject analysis set type	Per protocol

Subject analysis set description:

Each volunteer had proximal FTB bilaterally. For the discomfort the volunteer was asked to give one total score for the discomfort during the proximal FTB performance.

Subject analysis set title	Distal FTB right + left side
Subject analysis set type	Per protocol

Subject analysis set description:

Each volunteer had distal FTB bilaterally. For the discomfort the volunteer was asked to give one total score for the discomfort during the distal FTB performance.

Primary: Success rate of complete anesthesia of the midline skin incision after proximal FTB combined with IFCNB compared to proximal FTB alone

End point title	Success rate of complete anesthesia of the midline skin incision after proximal FTB combined with IFCNB compared to proximal FTB alone

End point description:

Pinprick was performed 30 min after performance of the last block. Pinprick was performed using a sterile neurological examination pin (Neuropen, Owen Mumford, UK). Cutaneous anesthesia was graded as either complete or incomplete/absent.

End point type	Primary

End point timeframe:

Standard midline incision for TKA drawn with UV pen at baseline. Pinprick testing performed 30 min after block performance.

End point values	Active proximal FTB + active IFCNB	Active proximal FTB + placebo IFCNB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: No unit				
Complete anesthesia of the incision line	15	4		
Incomplete anesthesia of the incision line	5	16		

Statistical analyses

Statistical analysis title	Primary outcome - Fischer's exact

Statistical analysis description:

Fischer's exact test

Comparison groups	Active proximal FTB + active IFCNB v Active proximal FTB + placebo IFCNB
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Fisher exact

Secondary: Success rate of complete anesthesia of the incision line with distal FTB combined with IFCNB compared to distal FTB alone

End point title	Success rate of complete anesthesia of the incision line with distal FTB combined with IFCNB compared to distal FTB alone

End point description:

End point type	Secondary

End point timeframe:

Pinprick performed 30 minutes after the last block performance

End point values	Active distal FTB + active IFCNB	Active distal FTB + placebo IFCNB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: No unit				
Complete anesthesia of the incision line	7	1		
Incomplete anesthesia of the incision line	13	19		

Statistical analyses

Statistical analysis title	Secondary outcome - Fischer's exact
Comparison groups	Active distal FTB + active IFCNB v Active distal FTB + placebo IFCNB
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Fisher exact

Secondary: Success rate of complete anesthesia of the incision line with proximal FTB and IFCNB compared to distal FTB and IFCNB

End point title	Success rate of complete anesthesia of the incision line with proximal FTB and IFCNB compared to distal FTB and IFCNB

End point description:

End point type	Secondary

End point timeframe:

Pinprick performed 30 min after block performance

End point values	Active proximal FTB + active IFCNB	Active distal FTB + active IFCNB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: No unit				
Complete cutaneous anesthesia of the incision line	15	7		
Incomplete cutaneous anesthesia of the incision	5	20		

Statistical analyses

Statistical analysis title	Secondary outcome - Fischer's exact
Comparison groups	Active distal FTB + active IFCNB v Active proximal FTB + active IFCNB
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Fisher exact

Secondary: Frequency of a non-anesthetized gap on the anteromedial side between the expected areas of cutaneous anesthesia after proximal vs. distal FTB both combined with an IFCNB

End point title	Frequency of a non-anesthetized gap on the anteromedial side between the expected areas of cutaneous anesthesia after proximal vs. distal FTB both combined with an IFCNB

End point description:

End point type	Secondary

End point timeframe:

Pinprick performed 30 min after block placement

End point values	Active proximal FTB + active IFCNB	Active distal FTB + active IFCNB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: No unit				
Gap at the anteromedial side	2	17		
No gap at the anteromedial side	18	3		

Statistical analyses

Statistical analysis title	Secondary outcome - Fischer's exact
Comparison groups	Active distal FTB + active IFCNB v Active proximal FTB + active IFCNB
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0
Method	Fisher exact

Secondary: Maximal extension of the cutaneous area of anesthesia

End point title	Maximal extension of the cutaneous area of anesthesia

End point description:

Maximal extension of the cutaneous area of anesthesia after proximal and distal FTB measured as the direct distance on a straight line from the tibial tuberosity to the point of maximal extension in the proximal, distal, medial and lateral direction.

End point type	Secondary

End point timeframe:

Measured after pinprick testing at the data collection station.

End point values	Active proximal FTB (before IFCNB)	Active distal FTB (before IFCNB)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[1]	40[2]		
Units: centimeter				
arithmetic mean (standard deviation)				
Maximal proximal extension	26.1 (± 7.9)	12.1 (± 7.8)		
Maximal distal extension	34.0 (± 4.9)	33.7 (± 6.0)		
Maximal medial extension	22.7 (± 4.6)	18.1 (± 4.4)		
Maximal lateral extension	9.9 (± 1.9)	10.0 (± 2.7)		

Notes:

[1] - 40 legs

[2] - 40 legs

Statistical analyses

No statistical analyses for this end point

Secondary: Injection point for IFCNB

End point title	Injection point for IFCNB

End point description:

Distance from the intersection of the inguinal crease and the femoral artery to the injection point for IFCNB

End point type	Secondary

End point timeframe:

Measured just before block performance

End point values	IFCNB right side	IFCNB left side		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[3]	40[4]		
Units: centimeter				
arithmetic mean (standard deviation)	9.8 (± 1.8)	9.3 (± 2.0)		

Notes:

[3] - 40 legs

[4] - 40 legs

Statistical analyses

No statistical analyses for this end point

Secondary: Block performance time IFCNB

End point title	Block performance time IFCNB

End point description:

End point type	Secondary

End point timeframe:

Block performance time defined as the time from the start of ultrasound scanning to the end of the injection

End point values	IFCNB right side	IFCNB left side		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[5]	40[6]		
Units: minute				
arithmetic mean (standard deviation)	3.2 (± 0.8)	3.4 (± 1.0)		

Notes:

[5] - 40 legs

[6] - 40 legs

Statistical analyses

No statistical analyses for this end point

Secondary: Block performance time proximal FTB

End point title	Block performance time proximal FTB

End point description:

End point type	Secondary

End point timeframe:

Block performance time defined as the time from the start of ultrasound scanning to the end of the injection

End point values	Proximal FTB right side	Proximal FTB left side		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[7]	40[8]		
Units: minute				
arithmetic mean (standard deviation)	2.2 (± 0.8)	2.4 (± 0.8)		

Notes:

[7] - 40 legs

[8] - 40 legs

Statistical analyses

No statistical analyses for this end point

Secondary: Block performance time distal FTB

End point title	Block performance time distal FTB

End point description:

End point type	Secondary

End point timeframe:

Block performance time defined as the time from the start of ultrasound scanning to the end of the injection

End point values	Distal FTB right side	Distal FTB left side		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[9]	40[10]		
Units: minute				
arithmetic mean (standard deviation)	2.1 (± 0.7)	2.3 (± 0.7)		

Notes:

[9] - 40 legs

[10] - 40 legs

Statistical analyses

No statistical analyses for this end point

Secondary: Discomfort during IFCNB performance

End point title	Discomfort during IFCNB performance

End point description:

Volunteers were asked to score the discomfort/pain during the performance of the IFCNB. Volunteers were asked to give one total score including both sides. Discomfort/pain was scored on the NRS 0-10

End point type	Secondary

End point timeframe:

Evaluated after performance of the last nerve block

End point values	IFCNB right + left side			
Subject group type	Subject analysis set			
Number of subjects analysed	40[11]			
Units: NRS 0-10				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)			

Notes:

[11] - Each volunteer gave a total score including both right and left leg

Statistical analyses

No statistical analyses for this end point

Secondary: Discomfort during proximal FTB performance

End point title	Discomfort during proximal FTB performance

End point description:

Volunteers were asked to score the discomfort/pain during the performance of the proximal FTB. Volunteers were asked to give one total score including both sides. Discomfort/pain was scored on the NRS 0-10.

End point type	Secondary

End point timeframe:

Evaluated after performance of the last nerve block

End point values	Proximal FTB right + left side			
Subject group type	Subject analysis set			
Number of subjects analysed	40[12]			
Units: NRS 0-10				
median (inter-quartile range (Q1-Q3))	4 (2.5 to 5.5)			

Notes:

[12] - Each volunteer gave a total score including both right and left leg

Statistical analyses

No statistical analyses for this end point

Secondary: Discomfort during distal FTB performance

End point title	Discomfort during distal FTB performance

End point description:

Volunteers were asked to score the discomfort/pain during the performance of the distal FTB. Volunteers were asked to give one total score including both sides. Discomfort/pain was scored on the NRS 0-10.

End point type	Secondary

End point timeframe:

Evaluated after performance of the last block

End point values	Distal FTB right + left side			
Subject group type	Subject analysis set			
Number of subjects analysed	40[13]			
Units: NRS 0-10				
median (inter-quartile range (Q1-Q3))	5 (3 to 6)			

Notes:

[13] - Each volunteer gave a total score including both right and left leg

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in knee extension force after IFCNB

End point title	Reduction in knee extension force after IFCNB

End point description:

Reduction of maximal force of knee extension after IFCNB

End point type	Secondary

End point timeframe:

Knee extension force (measured as maximal voluntary isometric force (MVIC)). MVIC was measured at baseline, after the first block session (proximal + distal FTB) and after the second block session (IFCNB)

End point values	Active proximal FTB + active IFCNB	Active distal FTB + active IFCNB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: newton				
median (standard deviation)				
MVIC knee extension before IFCNB	252.6 (± 142.6)	332.1 (± 120.7)		
MVIC knee extension after IFCNB	237.6 (± 152.1)	314.8 (± 159.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From time of inclusion and up until 24 hours after inclusion	
Adverse event reporting additional description:	
All adverse events were evaluated and followed-up by a specialist anesthetist.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Randomization group 1
Reporting group description:	
Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine). Leg leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline).	
Reporting group title	Randomization group 2
Reporting group description:	
Right leg: ACTIVE distal FTB (20 ml ropivacaine) +PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline). Left leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine).	
Reporting group title	Randomization group 3
Reporting group description:	
Right leg: PLACEBO distal FTB (20 ml saline) + ACTIVE proximal FTB (10 ml ropivacaine) + ACTIVE IFCNB (10 ml ropivacaine) Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + PLACEBO IFCNB (10 ml saline)	
Reporting group title	Randomization group 4
Reporting group description:	
Right leg: PLACEBO distal FTB (20 ml saline) +ACTIVE proximal FTB (10 ml ropivacaine) + PLACEBO IFCNB (10 ml saline) Left leg: ACTIVE distal FTB (20 ml ropivacaine) + PLACEBO proximal FTB (10 ml saline) + ACTIVE IFCNB (10 ml ropivacaine)	

Serious adverse events	Randomization group 1	Randomization group 2	Randomization group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Randomization group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Randomization group 1	Randomization group 2	Randomization group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
General disorders and administration site conditions			
Dizziness	Additional description: Caused by orthostatic hypotension		
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reduced cutaneous sensation	Additional description: Resolved spontaneously the next day. No sequelae.		
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Reduced muscle strength	Additional description: Resolved spontaneously the next day. No sequelae.		
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Randomization group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
General disorders and administration site conditions			
Dizziness	Additional description: Caused by orthostatic hypotension		
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reduced cutaneous sensation	Additional description: Resolved spontaneously the next day. No sequelae.		
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reduced muscle strength	Additional description: Resolved spontaneously the next day. No sequelae.		
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2019	Amendment approved by the Ethics Committee March 8, 2019 and by the Danish Medicines Agency March 15, 2019. The amendment was approved before recruitment was started. The amendment was made to improve the design of the study and ropivacaine was changed from 7.5 mg/ml to 5 mg/ml to reduce the accumulated dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported