Clinical trial results:
Opioid free anesthesia in total hip arthroplasty. A randomized, controlled and triple-blind clinical trial.

Summary

EudraCT number	2021-003703-18
Trial protocol	FR
Global end of trial date	02 February 2023

Results information

Result version number	v1 (current)
This version publication date	06 May 2023
First version publication date	06 May 2023

Trial information

Trial identification

Sponsor protocol code	2021/04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05072704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CMC Ambroise Paré
Sponsor organisation address	27 boulevard Victor Hugo, Neuilly-sur-Seine, France, 92200
Public contact	Service Recherche Clinique, CMC Ambroise Paré, +33 146415079, recherche@clinique-a-pare.fr
Scientific contact	Service Recherche Clinique, CMC Ambroise Paré, +33 146415079, recherche@clinique-a-pare.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	30 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2023
Global end of trial reached?	Yes
Global end of trial date	02 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the benefit of OFA strategy with dexmedetomidine infusion in postoperative analgesia defined by the oxycodone consumption in the first 24 hours after outpatient total hip arthroplasty.

Protection of trial subjects:

This clinical trial was approved by a Committee for Protection of Human Subjects (CPP Sud Est V - 21-PARE-01 N°SI RIPH 2G : 21.01512) and the french national agency for medicines and health products safety (ANSM MEDAECNAT-2021-07-0023_2021-003703-18). The trial was conducted in accordance with the Declaration of Helsinki and the Good Clinical Practice. 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	03 February 2022
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: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	52
From 65 to 84 years	27

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients were included from February 2022 to February 2023.
Patients scheduled for outpatient primary total hip arthroplasty under general anesthesia with laryngeal mask were informed of the study protocol during the anesthesia consultation. They were included on the day of the surgery during preanesthesia visit.

Pre-assignment

Screening details:

Exclusion criteria : refusal to participate, age < 18 years, hip revision surgery, heart rate < 60 bpm, chronic pain syndrom requiring preoperative morphine use (class 3), contraindications to one or more medications of the protocol, contraindication to laryngeal mask

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control Group

Arm description:

Usual anesthesia strategy with opioids (sufentanil)

Arm type	Active comparator
Investigational medicinal product name	Sufentanil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Pre-operative injection of sufentanil 10µg in 2ml of normal saline on induction of anesthesia + per-operative injection of sufentanil 5µg in 1ml of normal saline during the surgery if needed.

Arm title	OFA Group

Arm description:

Opioid-free anesthesia strategy: using dexmedetomidine

Arm type	Experimental
Investigational medicinal product name	Dexmedetomidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Pre-operative infusion of dexmedetomidine 1µg/kg in 100ml of normal saline before surgery + per-operative infusion of dexmedetomidine 0.4 µg/kg in 100ml of normal saline during the surgery if needed.

Number of subjects in period 1	Control Group	OFA Group
Started	40	40
Completed	40	40

Baseline characteristics

Reporting groups	
Reporting group title	Control Group
Reporting group description:	
Usual anesthesia strategy with opioids (sufentanil)	
Reporting group title	OFA Group
Reporting group description:	
Opioid-free anesthesia strategy: using dexmedetomidine	

Reporting group values	Control Group	OFA Group	Total
Number of subjects	40	40	80
Age categorical Units: Subjects			
Adults (18-64 years)	31	21	52
From 65-84 years	8	19	27
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	59.5	60.3	
standard deviation	± 8.3	± 12.6	-
Gender categorical Units: Subjects			
Male	24	31	55
Female	16	9	25
Surgical approach to the hip Units: Subjects			
Anterior	11	17	28
Posterolateral	29	23	52
Need for an additional injection (sufentanil or dexmedetomidine) during surgery Units: Subjects			
Yes	16	16	32
No	24	24	48
BMI Units: kilogram(s)/square metre			
arithmetic mean	26.5	24.8	
standard deviation	± 3.2	± 3.3	-
Surgery time Units: minute			
median	50	50	
inter-quartile range (Q1-Q3)	45 to 60	45 to 56	-
Propofol Units: milligram(s)			
median	1200	1235	
inter-quartile range (Q1-Q3)	1150 to 1525	1015 to 1425	-

End points

End points reporting groups	
Reporting group title	Control Group
Reporting group description: Usual anesthesia strategy with opioids (sufentanil)	
Reporting group title	OFA Group
Reporting group description: Opioid-free anesthesia strategy: using dexmedetomidine	

Primary: Postoperative analgesia, defined by the oxycodone consumption in the first 24 hours post-surgery	
End point title	Postoperative analgesia, defined by the oxycodone consumption in the first 24 hours post-surgery
End point description: Postoperative cumulated dose of oxycodone in oral morphine equivalent (mg)	
End point type	Primary
End point timeframe: From the arrival time in post-anesthesia care unit (PACU) to 24h after surgery	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))				
Cumulative OME at H24, mg	12 (0 to 29)	16 (0 to 30)		

Statistical analyses

Statistical analysis title	Cumulative OME at 24h
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Wilcoxon (Mann-Whitney)

Secondary: Analgesia in post-anesthesia care unit (PACU)	
End point title	Analgesia in post-anesthesia care unit (PACU)
End point description: Total amount of oxycodone (mg) administered in PACU	

End point type	Secondary
End point timeframe: PACU stay	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))				
Cumulative OME in PACU, mg	7 (0 to 18)	6 (0 to 12)		

Statistical analyses

Statistical analysis title	Cumulative OME in PACU
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Wilcoxon (Mann-Whitney)

Secondary: Postoperative pain at rest

End point title	Postoperative pain at rest
End point description: Postoperative pain at rest (numeric rating scale ranging from 0 to 10: 0= no pain; 10= worst imaginable pain)	
End point type	Secondary
End point timeframe: 24h after surgery	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[1]	40[2]		
Units: No unit				
median (inter-quartile range (Q1-Q3))				
VRS at H0	2.0 (0.0 to 6.0)	1.0 (0.0 to 5.0)		
VRSmax during PACU stay	5.0 (3.0 to 7.0)	5.0 (2.2 to 5.0)		
VRS at discharge from the PACU	2.0 (1.0 to 3.0)	2.0 (0.0 to 3.0)		
VRS at H6	0.0 (0.0 to 0.8)	0.0 (0.0 to 1.0)		
VRS at H12	2.0 (1.0 to 3.0)	2.0 (1.0 to 4.0)		
VRS at H18	2.0 (1.0 to 3.0)	2.5 (2.0 to 4.0)		

VRS at H24	2.0 (1.0 to 3.0)	2.0 (2.0 to 3.0)		

Notes:

[1] - 1 missing data in Control group for VRS at H0

[2] - OFA Group : 2 missing data for VRS at H0 ; 1 missing data for VRS at discharge from the PACU

Statistical analyses

Statistical analysis title	VRS at H0
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRSmax during PACU stay
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at discharge from the PACU
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at H6
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at H12

Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at H18
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at H24
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Wilcoxon (Mann-Whitney)

Secondary: Postoperative pain at walk	
End point title	Postoperative pain at walk
End point description:	
Postoperative pain at mobilization (numeric rating scale ranging from 0 to 10 : 0 = no pain; 10 = worst imaginable pain)	
End point type	Secondary
End point timeframe:	
Days 0 and 1	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: No unit				
median (inter-quartile range (Q1-Q3))				
VRS at Day0 (operating day)	1.0 (0.0 to 3.0)	2.0 (0.0 to 3.0)		
VRS at Day1	2.0 (1.0 to 3.0)	3.0 (1.2 to 3.8)		

Statistical analyses

Statistical analysis title	VRS at Day0 (Operating day)
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	VRS at Day1
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Wilcoxon (Mann-Whitney)

Secondary: Length of stay in post-anesthesia care unit (PACU)	
End point title	Length of stay in post-anesthesia care unit (PACU)
End point description: Duration of PACU stay (min)	
End point type	Secondary
End point timeframe: Postoperative period : from the arrival in PACU to the discharge	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: minute				
median (inter-quartile range (Q1-Q3))				
PACU time, min	92 (82 to 109)	101 (81 to 127)		

Statistical analyses

Statistical analysis title	Duration of PACU stay (min)
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Wilcoxon (Mann-Whitney)

Secondary: Time to recover the ability to walk	
End point title	Time to recover the ability to walk
End point description: Duration for recovery the ability to walk (min)	
End point type	Secondary
End point timeframe: Postoperative period : from the arrival in PACU to the first successful walk test	

End point values	Control Group	OFA Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: minute				
arithmetic mean (standard deviation)				
Walking recovery time, min	240 (± 46)	225 (± 59)		

Statistical analyses

Statistical analysis title	Duration for recovery the ability to walk (min)
Comparison groups	Control Group v OFA Group
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From time of inclusion to the end of the study for the subject	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1
Reporting groups	
Reporting group title	Control Group
Reporting group description: Usual anesthesia strategy with opioids (sufentanil)	
Reporting group title	OFA Group
Reporting group description: Opioid-free anesthesia strategy: using dexmedetomidine	

Serious adverse events	Control Group	OFA Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Severe hypotension	Additional description: systolic arterial pressure < 70 mmHg		
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Control Group	OFA Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 40 (95.00%)	32 / 40 (80.00%)	
Injury, poisoning and procedural complications			
Bleeding			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	0	
Laryngospasm			

subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Nausea and/or vomiting			
subjects affected / exposed	3 / 40 (7.50%)	1 / 40 (2.50%)	
occurrences (all)	3	1	
Vascular disorders			
Hypotension	Additional description: systolic arterial pressure < 90 mmHg or requiring treatment		
subjects affected / exposed	19 / 40 (47.50%)	13 / 40 (32.50%)	
occurrences (all)	27	20	
Hypertension	Additional description: systolic arterial pressure > 160 mmHg or requiring treatment		
subjects affected / exposed	21 / 40 (52.50%)	20 / 40 (50.00%)	
occurrences (all)	21	21	
Cardiac disorders			
Bradycardia	Additional description: heart rate < 50 bpm or requiring treatment		
subjects affected / exposed	6 / 40 (15.00%)	9 / 40 (22.50%)	
occurrences (all)	6	12	
Surgical and medical procedures			
Prolonged hospitalization			
subjects affected / exposed	4 / 40 (10.00%)	0 / 40 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	8 / 40 (20.00%)	2 / 40 (5.00%)	
occurrences (all)	10	2	
Renal and urinary disorders			
Micturition disorder			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Psychiatric disorders			
Drowsiness			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Low back pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	

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

None reported