# 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<br>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<br>Units: years | | | |
| arithmetic mean | 59.5 | 60.3 | |
| standard deviation | ± 8.3 | ± 12.6 | - |
| Gender categorical<br>Units: Subjects | | | |
| Male | 24 | 31 | 55 |
| Female | 16 | 9 | 25 |
| Surgical approach to the hip<br>Units: Subjects | | | |
| Anterior | 11 | 17 | 28 |
| Posterolateral | 29 | 23 | 52 |
| Need for an additional injection (sufentanil or dexmedetomidine) during surgery<br>Units: Subjects | | | |
| Yes | 16 | 16 | 32 |
| No | 24 | 24 | 48 |
| BMI<br>Units: kilogram(s)/square metre | | | |
| arithmetic mean | 26.5 | 24.8 | |
| standard deviation | ± 3.2 | ± 3.3 | - |
| Surgery time<br>Units: minute | | | |
| median | 50 | 50 | |
| inter-quartile range (Q1-Q3) | 45 to 60 | 45 to 56 | - |
| Propofol<br>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:<br>Usual anesthesia strategy with opioids (sufentanil) | |
| Reporting group title | OFA Group |
| Reporting group description:<br>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:<br>Postoperative cumulated dose of oxycodone in oral morphine equivalent (mg) | |
| End point type | Primary |
| End point timeframe:<br>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:<br>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:<br>Duration of PACU stay (min) | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>Duration for recovery the ability to walk (min) | |
| End point type | Secondary |
| End point timeframe:<br>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