Clinical trial results:
Risk factors and Prevention of severe Pain upon cessation of a peripheral nerve block.
A prospective randomized study in ambulatory patients undergoing upper limb bone surgery under single shot axillary plexus block.

Summary

EudraCT number	2019-001079-35
Trial protocol	BE
Global end of trial date	21 April 2021

Results information

Result version number	v1 (current)
This version publication date	25 December 2022
First version publication date	25 December 2022
Summary attachment (see zip file)	PRPK Summary Results (PRPK article BJA.pdf)

Trial information

Trial identification

Sponsor protocol code	PRPK

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cliniques Universitaires Saint Luc
Sponsor organisation address	Avenue Hippocrate, 10, Bruxelles, Belgium, 1200
Public contact	Lavand'homme Patricia, Cliniques Universitaires Saint Luc, patricia.lavandhomme@saintluc.uclouvain.be
Scientific contact	Lavand'homme Patricia, Cliniques Universitaires Saint Luc, patricia.lavandhomme@saintluc.uclouvain.be

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	29 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study will assess pain and recovery after single shot axillary plexus block in ambulatory patients undergoing upper limb bone surgery. We will try to identify risk factors for severe pain when the PNB wears off.

Protection of trial subjects:

Insurrance was taken. Except for the study specific interventions, patients were treated as per standard of care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2020
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	Belgium: 110
Worldwide total number of subjects	110
EEA total number of subjects	110

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)	86
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients between 18 and 80 yr of age scheduled for elective ambulatory upper limb surgery (elbow and under) under anaxillary plexus block were prospectively enrolled between January 2019 and March 2021. Patients were recruited during preoperative surgical or anaesthesia visit.

Pre-assignment

Screening details:

Incl. Crit.:
- ambulatory upper limb bone surgery done under axillary PNB
- age: 18 to 75 yrs old

Excl. Crit:
- contraindication to: use of ketamine or regular use of usual postoperative analgesics
- pregnant woman
- diabetic or vascular patient
- cognitive disorder
- inhability to answer perioperative questionnaires

Pre-assignment period milestones

Number of subjects started	110
Number of subjects completed	109

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Lost of FU: 1

Period 1

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

Blinding implementation details:

Randomization preparation and conservation by pharmacy of anonymized syringes in anonymous envelopes.
The syringes were given to the anesthetist doctor who remainded blinded, and were injected in the intervention room under standard monitoring.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

Group injected with 0.3 mg/kg intravenous ketamine diluted into 10mL saline

Arm type	Experimental
Investigational medicinal product name	Ketamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

0.3 mg/kg intravenous ketamine diluted into 10mL saline - slow intravenous injection after the realization of PNB, before tourniquet set up and beginning of surgery.

Investigational medicinal product name	NaCL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

0.3 mg/kg intravenous ketamine diluted into 10mL saline - slow intravenous injection after the realization of PNB, before tourniquet set up and beginning of surgery.

Arm title	Placebo

Arm description:

Slow intravenous injection of 10 mL 0.9% saline after the realization of PNB, before tourniquet set up and beginning of surgery

Arm type	Placebo
Investigational medicinal product name	NaCL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

10 mL 0.9% saline solution (NaCL)

Number of subjects in period 1[1]	Ketamine	Placebo
Started	54	55
Completed	54	55

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Overall trial results are showing only data collected on patients who completed the study.

Baseline characteristics

Reporting groups	
Reporting group title	Ketamine
Reporting group description:	
Group injected with 0.3 mg/kg intravenous ketamine diluted into 10mL saline	
Reporting group title	Placebo
Reporting group description:	
Slow intravenous injection of 10 mL 0.9% saline after the realization of PNB, before tourniquet set up and beginning of surgery	

Reporting group values	Ketamine	Placebo	Total
Number of subjects	54	55	109
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			
Units: years			
arithmetic mean	51	52	
standard deviation	± 16	± 18	-
Gender categorical			
Units: Subjects			
Female	29	28	57
Male	25	27	52

End points

End points reporting groups

Reporting group title	Ketamine
Reporting group description:	
Group injected with 0.3 mg/kg intravenous ketamine diluted into 10mL saline	
Reporting group title	Placebo
Reporting group description:	
Slow intravenous injection of 10 mL 0.9% saline after the realization of PNB, before tourniquet set up and beginning of surgery	

Primary: Incidence of Rebound Pain after upper limb surgery under axillary plexus block

End point title	Incidence of Rebound Pain after upper limb surgery under axillary plexus block[1]
End point description:	
End point type	Primary
End point timeframe:	
Post-operative - When block wear off	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: For the incidence of rebound pain, ratio/percentages were used.

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Incidence RP (n)				
With Rebound Pain when block wear off	18	26		
Without Rebound Pain when block wear off	36	29		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Overall trial

Adverse event reporting additional description:

From enrollment untill completion of the study.

Assessment type	Systematic

Dictionary used

Dictionary name	ICD 10 - Enfglish
Dictionary version	2015

Reporting groups

Reporting group title	Ketamine

Reporting group description:

Group injected with 0.3 mg/kg intravenous ketamine diluted into 10mL saline

Reporting group title	Placebo

Reporting group description:

Slow intravenous injection of 10 mL 0.9% saline after the realization of PNB, before tourniquet set up and beginning of surgery

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 information about non-serious adverse events were received.

Serious adverse events	Ketamine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Anaphylactic reaction	Additional description: Anaphylactic reaction on standard of care administration of NSAIDs. Unrelated to the study procedures. Event resolved without sequelae.		
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ketamine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35219449