Clinical trial results:
Continous wound infiltration after hallux valgus surgery

Summary

EudraCT number	2013-005106-64
Trial protocol	AT
Global end of trial date	30 April 2017

Results information

Result version number	v1 (current)
This version publication date	17 July 2020
First version publication date	17 July 2020
Summary attachment (see zip file)	DSUR CWI-HVS (DSUR CWI-HVS 2017.docx)

Trial information

Trial identification

Sponsor protocol code	CWI-HVS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02182999
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Christoph-Probst-Platz 1, Innrain 52 A, Innsbruck, Austria, 6020
Public contact	Univ.Prof. Dr. Martin Krismer , Medical University Innsbruck University Hospital for Orthopaedics Anichstrasse 35 6020 Innsbruck, 43 512/504-22691, martin.krismer@tirol-kliniken.at
Scientific contact	Univ.Prof. Dr. Martin Krismer , Medical University Innsbruck University Hospital for Orthopaedics Anichstrasse 35 6020 Innsbruck, 43 512/504-22691, martin.krismer@tirol-kliniken.at

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 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2017
Global end of trial reached?	Yes
Global end of trial date	30 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to investigate the effect of continous wound infiltration with long-lasting local anesthetics in comparison to standard pain management after elective distal metatarsal osteotomy for postoperative pain control.

Protection of trial subjects:

Patients received 1.3 mg hydromorphone (Hydal, Mundipharma GmbH, Vienna, Austria) as a rescue medication for NRS (numeric rating scale; 1-10, higher numbers indicating increasing pain level) pain score greater than 3.

Background therapy:

For postoperative pain management, naproxen 500 mg (Naprobene; ratiopharm Arzneimittel Vertriebs-GmbH, Vienna, Austria) was administered twice a day. Patients were routinely discharged the second day after surgery and 500 mg of naproxen twice a day was prescribed for 5 days.

Evidence for comparator:

Hallux valgus surgery is usually associated with significant postoperative pain, especially during the first 24 hours postoperatively. Previous studies showed that the CWI (continuous wound infiltration / infusion) of local anesthetics provides sufficient postoperative analgesia and reduces postoperative narcotic consumption without an increased risk of complications.

Actual start date of recruitment	03 March 2014
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	Austria: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	35
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients undergoing a distal metatarsal osteotomy and lateral release with or without concomitant osteotomy of the proximal phalanx of the greater toe (Akin osteotomy) for idiopathic hallux valgus deformity at the Department of Orthopedic Surgery, Medical University of Innsbruck, between May 2014 and March 2017 were screened for eligibility.

Pre-assignment

Screening details:

A total of 294 osteotomies of the first metatarsal were performed for idiopathic hallux valgus deformity at the Department of Orthopedic Surgery, Medical University of Innsbruck, between May 2014 and March 2017. After screening for eligibility, 50 patients were enrolled in the study.

Period 1

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

Blinding implementation details:

A randomization sequence was generated by computer software (http://www.randomizer.org). A randomization list from 1 to 50 was created, each number encoding for treatment or placebo group. The numbers were placed in 50 individual sealed opaque envelopes marked 1 to 50. The randomization list was stored in a locked room and could only be accessed by one independent member of the nursing staff, who prepared the study medication but did not take part in patient care.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment goup

Arm description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).

Arm type	Active comparator
Investigational medicinal product name	Ropinaest®
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine
2 mg/mL (Gebro GmbH, 6391 Fieberbrunn, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).

Arm title	Placebo group

Arm description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).

Arm type	Placebo

Investigational medicinal product name	Physiologic salt solution
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with Physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).

Number of subjects in period 1	Treatment goup	Placebo group
Started	25	25
Completed	22	20
Not completed	3	5
Dislocation of catheter	2	3
Removal of catheter due to local dysesthesia	1	-
Intraoperative conversion to arthrodesis	-	1
Revision of catheter fixed by suture	-	1

Period 2

Period 2 title	Follow-up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

A randomization sequence was generated by computer software (http://www.randomizer.org). A randomization list from 1 to 50 was created, each number encoding for treatment or placebo group. The numbers were placed in 50 individual sealed opaque envelopes marked 1 to 50. The randomization list was stored in a locked room and could only be accessed by one independent member of the nursing staff, who prepared the study medication but did not take part in patient care.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment goup

Arm description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).

Arm type	Active comparator

Investigational medicinal product name	Ropinaest®
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine
2 mg/mL (Gebro GmbH, 6391 Fieberbrunn, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).

Arm title	Placebo group

Arm description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).

Arm type	Placebo
Investigational medicinal product name	Physiologic salt solution
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with Physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).

Number of subjects in period 2	Treatment goup	Placebo group
Started	22	20
Completed	21	18
Not completed	1	2
Wound infection and dehiscence	-	1
Fracture of the first metatarsal	1	-
Rupture of flexor hallucis tendon	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment goup
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).	
Reporting group title	Placebo group
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).	

Reporting group values	Treatment goup	Placebo group	Total
Number of subjects	25	25	50
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	17	35
From 65-84 years	7	8	15
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	58.0	52.5	
standard deviation	± 13.1	± 17.2	-
Gender categorical			
Units: Subjects			
Female	20	20	40
Male	5	5	10

End points

End points reporting groups

Reporting group title	Treatment goup
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).	
Reporting group title	Placebo group
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).	
Reporting group title	Treatment goup
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).	
Reporting group title	Placebo group
Reporting group description:	
Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).	

Primary: Average pain level during the first 48 hours after surgery

End point title	Average pain level during the first 48 hours after surgery
End point description:	
The primary outcome parameters of this study were average pain and peak pain level on the verbal numeric rating scale (NRS; 1-10, higher numbers indicating increasing pain level) during the first 48 hours after surgery. NRS scores for pain were recorded by members of the nursing staff every 4 hours after the procedure until discharge, with the exception of the control at 4 am in the morning (16 hours, 40 hours), when most patients were asleep.	
End point type	Primary
End point timeframe:	
Day 1- day 3	

End point values	Treatment goup	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: NRS (Numeric Rating Scale)				
arithmetic mean (standard deviation)				
Average pain level	1.9 (± 0.8)	2.0 (± 0.7)		

Statistical analyses

Statistical analysis title	Pain level
Comparison groups	Placebo group v Treatment goup
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.596
Method	t-test, 2-sided

Primary: Peak pain level during the first 48 hours after surgery

End point title	Peak pain level during the first 48 hours after surgery

End point description:

The primary outcome parameters of this study were average pain and peak pain level on the verbal numeric rating scale (NRS; 1-10, higher numbers indicating increasing pain level) during the first 48 hours after surgery. NRS scores for pain were recorded by members of the nursing staff every 4 hours after the procedure until discharge, with the exception of the control at 4 am in the morning (16 hours, 40 hours), when most patients were asleep.

End point type	Primary

End point timeframe:

Day 1- day 3

End point values	Treatment goup	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: NRS (Numeric Rating Scale)				
arithmetic mean (standard deviation)				
Peak pain level	3.5 (± 2.0)	3.9 (± 1.7)		

Statistical analyses

Statistical analysis title	Peak pain level
Comparison groups	Treatment goup v Placebo group
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.353
Method	t-test, 2-sided

Secondary: Rescue medicaton during the first 48 hours after surgery

End point title	Rescue medicaton during the first 48 hours after surgery

End point description:

Patients received 1.3 mg hydromorphone (Hydal, Mundipharma GmbH, Vienna, Austria) as a rescue medication for NRS pain score greater than 3. Mean narcotic consumption during the first 48 hours after surgery did not differ significantly between both groups, although there was a trend toward a lower need for rescue medication in the treatment group compared with the control group.

End point type	Secondary

End point timeframe:

Day 1-day 3

End point values	Treatment goup	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: mg				
arithmetic mean (standard deviation)				
Rescue medication	1.4 (± 1.7)	2.5 (± 2.5)		

Statistical analyses

Statistical analysis title	Rescue medication
Comparison groups	Treatment goup v Placebo group
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.354
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

03.03.2014-30.04.2017

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Treatment goup

Reporting group description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with ropivacaine (Gebro GmbH, 6391 Fieberbrunn, Austria) 2 mg/mL to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Melsungen, Germany).

Reporting group title	Placebo group

Reporting group description:

Continuous wound infiltration catheter was placed in the dorsomedial skin incision, connected to the filter and filled with physiologic salt solution 9 mg/mL (Fresenius Kabi Austria GmbH; Graz, Austria) to allow for CWI at a rate of 2 mL/h for 24 hours via a perfusor (Perfusor compact; B. Braun Melsungen, Germany).

Serious adverse events	Treatment goup	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)	1 / 25 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Revision of catheter fixed by a suture			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of catheter due to local dysesthesia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Treatment goup	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 25 (8.00%)	3 / 25 (12.00%)	
Surgical and medical procedures			
Dislocation of cathether			
subjects affected / exposed	2 / 25 (8.00%)	3 / 25 (12.00%)	
occurrences (all)	5	5	

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/29073780