Clinical trial results:
Prospective, double-blind, randomised trial to assess the efficacy of continuous sciatic/posterior tibial nerve blockade via a neural sheath catheter in lower limb amputees

Summary

EudraCT number	2007-000619-27
Trial protocol	GB
Global end of trial date	30 April 2013

Results information

Result version number	v1 (current)
This version publication date	27 December 2019
First version publication date	27 December 2019

Trial information

Trial identification

Sponsor protocol code	56481676

Additional study identifiers

ISRCTN number	ISRCTN68691928
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospitals of Leicester NHS Trust
Sponsor organisation address	Research & Innovation, Trust HQ. Level 3 Balmoral Building. Leicester Royal Infirmary. , Leicester, United Kingdom, LE1 5WW
Public contact	Carolyn Maloney, University Hospitals of Leicester NHS Trust, +44 116 258 4109, carolyn.maloney@uhl-tr.nhs.uk
Scientific contact	Prof. Jonathan Thompson, University Hospitals of Leicester NHS Trust, jt23@le.ac.uk

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 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2013
Global end of trial reached?	Yes
Global end of trial date	30 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the effects of continuous peri- and post-operative sciatic/posterior tibial nerve blockade using a levobupivacaine infusion via a neural sheath catheter on late stump pain, phantom limb sensations and phantom limb pain.

Protection of trial subjects:

All trial subjects (including intervention and control groups) received patient-controlled analgesia with morphine. All patients had access to further escape medication according to the protocol as required

Background therapy:

Standardised surgery performed under standardised general anaesthesia

Evidence for comparator:

Pain scores, requirements for analgesia, quality of life questionnaires

Actual start date of recruitment	01 October 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	27

From 65 to 84 years	48
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

Recruitment October 2007 to March 2013. Single UK centre

Pre-assignment

Screening details:

All patients admitted to the vascular unit at Leicester Royal Infirmary and planned for major lower limb amputation surgery (due to vascular aetiology) were considered for inclusion

Period 1

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

Blinding implementation details:

Computer generated randomisation by an independent clinical trials unit

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention group

Arm description:

infusion of 0.125% Levobupivacaine at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.

Arm type	Experimental
Investigational medicinal product name	levobupivacaine 0.125%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Perineural use

Dosage and administration details:

infusion of 0.125% Levobupivacaine at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.

Arm title	placebo control arm

Arm description:

infusion of 0.9% saline at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.

Arm type	Placebo
Investigational medicinal product name	0.9% saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Perineural use

Dosage and administration details:

infusion of 0.9% saline at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.

Number of subjects in period 1	Intervention group	placebo control arm
Started	45	45
Completed	41	40
Not completed	4	5
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	-
Protocol deviation	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Recruitment

Reporting group description: -

Reporting group values	Recruitment	Total	
Number of subjects	90	90	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	27	27	
From 65-84 years	48	48	
85 years and over	15	15	
18 -100	0	0	
Adults aged 18-64	0	0	
Age continuous			
Female			
Units: years			
median	72		
inter-quartile range (Q1-Q3)	62 to 82	-	
Gender categorical			
Male			
Units: Subjects			
Female	32	32	
Male	58	58	

End points

End points reporting groups

Reporting group title	Intervention group
Reporting group description:	
infusion of 0.125% Levobupivacaine at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.	
Reporting group title	placebo control arm
Reporting group description:	
infusion of 0.9% saline at a rate of 8mls h-1 for 96hrs via a neural sheath catheter into the sciatic or posterior tibial nerve for above and below knee amputations respectively.	

Primary: Presence or absence of significant phantom limb pain

End point title	Presence or absence of significant phantom limb pain
End point description:	
End point type	Primary
End point timeframe:	
6 months after intervention	

End point values	Intervention group	placebo control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: number	7	8		

Statistical analyses

Statistical analysis title	chi squared test
Comparison groups	Intervention group v placebo control arm
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	OED
Dictionary version	1
Reporting groups	
Reporting group title	experimental
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	experimental	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 41 (53.66%)	24 / 43 (55.81%)	
number of deaths (all causes)	7	6	
number of deaths resulting from adverse events	7	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer metastatic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain Tumour			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis postoperative			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb ischemia			

subjects affected / exposed	3 / 41 (7.32%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Ischaemic small bowel			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
femoral and iliac vein thrombosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CVA			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Saddle embolus			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
messenteric vascular occlusion			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Revision of amputation	Additional description: Below knee to above knee amputations		
subjects affected / exposed	7 / 41 (17.07%)	5 / 43 (11.63%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
loop colostomy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMA Embolectomy			

subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amputation	Additional description: Vascular insufficiency left AKA		
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
left CFA endarterectomy and a left profundaplasty			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioplasty			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amputation of toes	Additional description: Debridement and amputation of 1st,2nd and 3rd toes		
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
iliac and profunda thrombectomy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
axillo femoral bypass.			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right hemicolectomy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

Recto vaginal fistula			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Exacerbation COPD			
subjects affected / exposed	2 / 41 (4.88%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
pulmonary embolism			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary nodules	Additional description: possible lung metastasis		
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Dementia			
subjects affected / exposed	2 / 41 (4.88%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	

disassociation disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
delirium			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 41 (0.00%)	4 / 43 (9.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosis postoperative			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac arrest			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

SVT			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ECG changes			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IHD			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
PR Bleeding			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: admitted with 24hr history of vomiting		
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
small bowel ischaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematemesis due to severe eosophagitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Elevated Liver function tests			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cellulitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema	Additional description: right leg		
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer	Additional description: Non healing leg Ulcer		
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peri orbital swelling			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stage 3 pressure sore			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Hairline pelvic fracture	Additional description: Fall leading to fracture		

subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bakers Cyst			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Amputation wound infection			
subjects affected / exposed	1 / 41 (2.44%)	6 / 43 (13.95%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Axillo femoral graft			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous ulceration infection			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected axillo femoral graft			
subjects affected / exposed	1 / 41 (2.44%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pressure sore infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 43 (2.33%)	
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: 0 %

Non-serious adverse events	experimental	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 41 (14.63%)	4 / 43 (9.30%)	
Gastrointestinal disorders			
nausea and vomiting			
subjects affected / exposed	6 / 41 (14.63%)	4 / 43 (9.30%)	
occurrences (all)	1	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