Clinical trial results:
Shamrock – Ultrasound/MR image fusion guided lumbar plexus blocks

Summary

EudraCT number	2015-005544-33
Trial protocol	DK
Global end of trial date	10 April 2016

Results information

Result version number	v1 (current)
This version publication date	16 December 2016
First version publication date	16 December 2016

Trial information

Trial identification

Sponsor protocol code	AUH-TFB-SR-ULMR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02718976
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Thomas Fichtner Bendtsen
Sponsor organisation address	Dep. of Anesthesiology and Intensive Care, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark, DK-8000
Public contact	Clinical Trial Info: Shamrock US/MRI, Thomas Fichtner Bendtsen, 45 51542997, tfb@dadlnet.dk
Scientific contact	Clinical Trial Info: Shamrock US/MRI, Thomas Fichtner Bendtsen, 45 51542997, tfb@dadlnet.dk

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	21 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2016
Global end of trial reached?	Yes
Global end of trial date	10 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess lumbar plexus block (L2-L4) of the femoral, obturator, and lateral femoral cutaneous nerves with ultrasound/MRI image fusion guided Shamrock method vs. ultrasound guided Shamrock method in a blinded, randomized controlled trial. The lumbar plexus block is assessed as motor block of the femoral and obturator nerves and sensory block of the lateral femoral cutaneous nerve in healthy volunteers.
As an exploratory analysis, patterns of injectate spread with MRI were examined.

Protection of trial subjects:

The trial subjects were asked about their general well-being and any prior disease and discomfort during enrollment and upon arrival to as well as departure from the trial venue on each experimental day.
The trial subjects were monitored with 3-lead electrocardiography, non-invasive blood pressure, and pulse oximetry from five minutes before the pre-scan to five minutes after completed intervention.
During each intervention, the research anesthetist and the assistent communicated with the trial subject reassuring his/her well-being. Immediately after completed intervention, the maximal discomfort of the trial subject during the procedure was assessed on a numeric rating scale (NRS 0-10). All trial subjects were observed for adverse reactions until the sensorimotor effects had worn off.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2016
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	Denmark: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All volunteers were recruited through a Danish website for research volunteers in the period 8 to 31 March 2016.

Pre-assignment

Screening details:

22 volunteers were screened and 22 volunteers were included in the study.

Period 1

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

Blinding implementation details:

In addition we strived to blind the trial subjects with identical trial setup.

Arms

Are arms mutually exclusive?	No
Arm title	Shamrock US/MRI

Arm description:

All included trial subjects received a lumbar plexus block with the Shamrock technique guided by ultrasound/MRI fusion either on the first or the second trial day (randomized).

Arm type	Experimental
Investigational medicinal product name	Lidokain-adrenalin SAD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

20 ml 2% lidocaine with 0.0005% adrenaline was injected.

Investigational medicinal product name	Dotarem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Perineural use

Dosage and administration details:

0.13 ml Dotarem (279.3 mg gadoterate meglumine) was added to the lidocaine-adrenaline prior to injection in order to enhance visualization of the anatomical spread of lidocaine-adrenaline on MRI after the intervention.

Arm title	Shamrock US

Arm description:

All included trial subjects received a lumbar plexus block with the Shamrock technique guided by ultrasound either on the first or the second trial day (randomized).

Arm type	Active comparator
Investigational medicinal product name	Lidokain-adrenalin SAD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:	
20 ml 2% lidocaine with 0.0005% adrenaline was injected.	
Investigational medicinal product name	Dotarem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Perineural use
Dosage and administration details:	
0.13 ml Dotarem (279.3 mg gadoterate meglumine) was added to the lidocaine-adrenaline prior to injection in order to enhance visualization of the anatomical spread of lidocaine-adrenaline on MRI after the intervention.	

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The observers and analysts of data were blinded and we strived to blind the trial subjects with identical trial setup and by not revealing the type (US/MRI or MRI guided) intervention during the trial.

Number of subjects in period 1	Shamrock US/MRI	Shamrock US
Started	22	22
Completed	22	22

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	22	22	
Age categorical Units: Subjects			
Adults (18-64 years)	22	22	
Age continuous Units: years			
median	22.5		
inter-quartile range (Q1-Q3)	22 to 24	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	12	12	
Weight Units: kg			
arithmetic mean	73		
standard deviation	± 8.8	-	
Height Units: cm			
arithmetic mean	177		
standard deviation	± 9.6	-	
Body mass index Units: kg/m2			
arithmetic mean	23.2		
standard deviation	± 2	-	

End points

End points reporting groups	
Reporting group title	Shamrock US/MRI
Reporting group description:	
All included trial subjects received a lumbar plexus block with the Shamrock technique guided by ultrasound/MRI fusion either on the first or the second trial day (randomized).	
Reporting group title	Shamrock US
Reporting group description:	
All included trial subjects received a lumbar plexus block with the Shamrock technique guided by ultrasound either on the first or the second trial day (randomized).	

Primary: Block success	
End point title	Block success
End point description:	
Proportion of trial subjects with successful lumbar plexus blockade. A block was considered successful when the subject had motor blockade of the femoral and obturator nerves and sensory blockade of the lateral femoral cutaneous nerve. Motor blockade was defined as post-block muscle force < baseline muscle force of knee extension (femoral nerve) and hip adduction (obturator nerve), respectively. Sensory blockade was defined as decreased or absent sensation for cold and/or pain.	
End point type	Primary
End point timeframe:	
Baseline muscle force and sensory for cold and pain was assessed upon arrival on the first experimental day. Post-block muscle force was assessed 60 min after and sensory blockade 70 min after completed intervention.	

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects	16	18		

Statistical analyses

Statistical analysis title	Block success
Comparison groups	Shamrock US/MRI v Shamrock US
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Mcnemar
Parameter estimate	Difference in paired proportions

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.17

Secondary: Motor block

End point title	Motor block

End point description:

Number of subjects with successful motor blockade of the femoral and obturator nerves, respectively. A successful motor blockade was defined as post-block muscle force < baseline muscle force of knee extension (femoral nerve) and hip adduction (obturator nerve), respectively.

End point type	Secondary

End point timeframe:

Baseline muscle force was assessed upon arrival on the first experimental day. Post-block muscle force was assessed 60 min after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Femoral nerve	19	21		
Obturator nerve	17	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Block preparation time

End point title	Block preparation time

End point description:

End point type	Secondary

End point timeframe:

Assessed prior to intervention. Defined as the time from placement of the subject on the bed to completed pre-scanning and co-registration of ultrasound and MRI.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: second				
median (inter-quartile range (Q1-Q3))	868 (661 to 947)	471 (396 to 631)		

Statistical analyses

No statistical analyses for this end point

Secondary: Block procedure time

End point title	Block procedure time

End point description:

End point type	Secondary

End point timeframe:

Assessed as the time from placement of the probe on the skin after completed preparations to withdrawal of the block needle after completed injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: second				
median (inter-quartile range (Q1-Q3))	438 (272 to 567)	396 (296 to 524)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lumbar plexus ultrasonographically visualized

End point title	Lumbar plexus ultrasonographically visualized

End point description:

End point type	Secondary

End point timeframe:

Assessed immediately prior to the injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: subjects	20	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal electrical nerve stimulation

End point title	Minimal electrical nerve stimulation

End point description:

The minimum electrical nerve stimulation level in mA required to trigger a response was measured in order to confirm the position of the block needle tip before injection.

End point type	Secondary

End point timeframe:

Assessed immediately prior to injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: mA				
median (inter-quartile range (Q1-Q3))	0.26 (0.24 to 0.28)	0.28 (0.26 to 0.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Response on electrical nerve stimulation

End point title	Response on electrical nerve stimulation

End point description:

End point type	Secondary

End point timeframe:

Assessed immediately prior to injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Quadriceps femoris	13	16		
Adductor	9	5		
Other motor	0	0		
Paresthesia	0	1		
None	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of needle insertions

End point title	Number of needle insertions

End point description:

The number of block needle insertions was defined as the number of retractions of the block needle followed by advancement regardless of the number of skin insertions.

End point type	Secondary

End point timeframe:

Counted from the start of the block procedure time to the end of injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Number				
median (inter-quartile range (Q1-Q3))	4 (2 to 5)	4.5 (3 to 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Needle insertion point from midline

End point title	Needle insertion point from midline

End point description:

The block needle insertion point was estimated as the horizontal distance (cm) from the needle insertion point in the skin to the lumbar midline.

End point type	Secondary

End point timeframe:

Measured immediately after completed injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: cm				
median (inter-quartile range (Q1-Q3))	5 (4 to 6)	5 (4 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Needle depth

End point title	Needle depth

End point description:

The distance from skin to the block needle tip was estimated as the distance (cm) from the block needle insertion point in the skin to the block needle tip gauged by reading of the cm markings on the needle shaft.

End point type	Secondary

End point timeframe:

Measured immediately prior to injection of study medicine.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: cm				
median (inter-quartile range (Q1-Q3))	8 (7 to 8)	8 (8 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Procedural discomfort

End point title	Procedural discomfort

End point description:

Assessed immediately after completed intervention.

End point type	Secondary

End point timeframe:

The trial subject's discomfort during block procedure was assessed on a numeric rating scale (NRS) 0-10, where 0 = no discomfort and 10 = worst possible discomfort.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: NRS units				
median (inter-quartile range (Q1-Q3))	4 (3 to 7)	4 (3 to 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in mean arterial pressure (MAP)

End point title	Change in mean arterial pressure (MAP)

End point description:

End point type	Secondary

End point timeframe:

ΔMAP was measured as the change of MAP from the time immediately prior to pre-scanning to 5 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: mmHg				
median (inter-quartile range (Q1-Q3))	-3 (-8 to 2)	-4 (-6 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Perineural spread of injectate

End point title	Perineural spread of injectate

End point description:

Perineural spread of local anesthetic was assessed as present when visual contact between the local anesthetic and the nerve on MRI was confirmed.

End point type	Secondary

End point timeframe:

Assessed by MRI recorded 15 min after completed injection.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Anterior ramus L1	0	0		
Anterior ramus L2	19	21		
Anterior ramus L3	17	18		
Anterior ramus L4	10	9		
Anterior ramus L5	1	1		
Femoral nerve	15	14		
Obturator nerve	14	15		
Lateral femoral cutaneous nerve	16	15		
Lumbosacral trunk	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Epidural spread of injectate

End point title	Epidural spread of injectate

End point description:

Epidural spread was assessed to be present when circumferential epidural spread of the injectate was observed on MRI and decreased or absent sensation for cold was observed in at least one pair of bilateral dermatomes during the sensory mapping.

End point type	Secondary

End point timeframe:

Epidural spread of local anesthetics was assessed on MRI sampled 15 minutes after completed intervention and during sensory mapping 70 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory blockade - Cold

End point title	Sensory blockade - Cold

End point description:

Sensory block for cold in the dermatomes Th8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for cold was decreased/absent.

End point type	Secondary

End point timeframe:

Assessed 70 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Th8	0	0		
Th9	0	0		
Th10	0	0		
Th11	0	1		
Th12	4	3		
L1	5	12		
L2	17	19		
L3	12	16		
L4	12	16		
L5	5	12		
S1	18	18		
S2	2	4		
S3	2	3		
Lateral femoral cutaneous nerve	19	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory blockade - Warmth

End point title	Sensory blockade - Warmth

End point description:

Sensory block for warmth in the dermatomes Th8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for warmth was decreased/absent.

End point type	Secondary

End point timeframe:

Assessed 70 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Th8	0	1		
Th9	0	1		
Th10	1	0		
Th11	0	1		
Th12	3	3		
L1	12	10		
L2	16	21		
L3	13	16		
L4	14	18		
L5	7	11		
S1	13	15		
S2	3	7		
S3	3	7		
Lateral femoral cutaneous nerve	17	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory blockade - Touch

End point title	Sensory blockade - Touch

End point description:

Sensory block for touch in the dermatomes Th8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for touch was decreased/absent.

End point type	Secondary

End point timeframe:

Assessed 70 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Th8	0	1		
Th9	0	0		
Th10	1	0		
Th11	0	0		
Th12	3	5		
L1	8	10		
L2	14	16		
L3	10	12		
L4	10	14		

L5	0	0		
S1	3	1		
S2	3	4		
S3	3	5		
Lateral femoral cutaneous nerve	16	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory blockade - Pain

End point title	Sensory blockade - Pain

End point description:

Sensory block for pinprick (pain) in the dermatomes Th8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for pinprick was decreased/absent.

End point type	Secondary

End point timeframe:

Assessed 70 minutes after completed intervention.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Subjects				
Th8	0	1		
Th9	0	0		
Th10	0	0		
Th11	0	0		
Th12	3	5		
L1	9	11		
L2	15	16		
L3	12	14		
L4	10	11		
L5	0	2		
S1	7	4		
S2	2	2		
S3	2	6		
Lateral femoral cutaneous nerve	16	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Cost-effectiveness

End point title	Cost-effectiveness

End point description:

Cost-effectiveness of the interventions was estimated as the difference in mean marginal cost for the ultrasound/MRI fusion vs. the ultrasound guided Shamrock technique.

End point type	Secondary

End point timeframe:

Calculated in the end of the data analysis after last subject last visit.

End point values	Shamrock US/MRI	Shamrock US		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: GBP				
number (not applicable)	17.64	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Continuous and systematic assessment of adverse events from upon arrival to discharge on each experimental day. All trial subjects were urged to self-report any adverse events between the experimental days and after discharge.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Shamrock US/MRI
Reporting group description: -	
Reporting group title	Shamrock US

Reporting group description: -

Serious adverse events	Shamrock US/MRI	Shamrock US	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events		0	

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

Non-serious adverse events	Shamrock US/MRI	Shamrock US	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 22 (13.64%)	4 / 22 (18.18%)	
Vascular disorders			
Tachycardia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Lightheadedness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Flushing			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Haematoma muscular			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	

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