Clinical trial results:
Shamrock versus Lumbar Ultrasound Trident – Ultrasound guided block of the lumbar plexus

Summary

EudraCT number	2013-005346-10
Trial protocol	DK
Global end of trial date	08 March 2015

Results information

Result version number	v1 (current)
This version publication date	23 March 2016
First version publication date	23 March 2016

Trial information

Trial identification

Sponsor protocol code	AUH-TFB-SR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02255591
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Thomas Fichtner Bendtsen
Sponsor organisation address	Dep. of Anaesthesiology and Intensive Care, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark, DK-8000
Public contact	Clinical Trial Info – Shamrock, Thomas Fichtner Bendtsen, +45 51542997, tfb@dadlnet.dk
Scientific contact	Clinical Trial Info – Shamrock, 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	15 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2015
Global end of trial reached?	Yes
Global end of trial date	08 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to complete a double-blinded randomized controlled trial with crossover design of a lumbar plexus block with the Shamrock technique versus the Lumbar Ultrasound Trident technique by estimating the time for performance of lumbar plexus block in healthy volunteers.

Protection of trial subjects:

The trial subjects were asked about general well-being and any prior disease and discomfort upon arrival to the trial venue.
The trial subjects were monitored with 3-lead electrocardiography, noninvasive pressure, and pulse oximetry from five minutes before the pre-scan to five minutes after completed intervention. During the intervention, the research anaesthesiologist and the assistent communicated with the trail subject reassuring the well-being of the trial subject. Immediately after completed intervention, trial subject discomfort during the procedure was assessed on a numeric rating scale (NRS 0-10).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2015
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20

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 from Feb 9, 2015 to Feb 24, 2015.

Pre-assignment

Screening details:

22 volunteers were screened and 20 volunteers were included in the study. One of the excluded screened subjects had a knee injury (exclusion criteria). One of the excluded screened subjects was not available for participation on the pre-set dates of the trial.

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, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Shamrock

Arm description:

All included trial subjects received a lumbar plexus block with the Shamrock technique 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 injection 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	Lumbar Ultrasound Trident (LUT)

Arm description:

All included trial subjects received a lumbar plexus block with the LUT technique 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 injection 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: All trial subjects and observers and analysts of data were blinded.
The principal investigator was also the anesthesiologist who performed all lumbar plexus blocks and could therefore not be blinded. The P.I. was not involved in collecting or analyzing data.

Number of subjects in period 1	Shamrock	Lumbar Ultrasound Trident (LUT)
Started	20	20
Completed	20	19
Not completed	0	1
No show (study-unrelated reason)	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
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			
median	22.5		
inter-quartile range (Q1-Q3)	22 to 24.5	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	20	20	
Weight Units: kg			
arithmetic mean	80.1		
standard deviation	± 7.8	-	
Height Units: cm			
median	185		
inter-quartile range (Q1-Q3)	183 to 187	-	
Body Mass Index (BMI) Units: kg/m2			
arithmetic mean	25.3		
standard deviation	± 2.9	-	

End points

End points reporting groups

Reporting group title	Shamrock
Reporting group description:	
All included trial subjects received a lumbar plexus block with the Shamrock technique either on the first or the second trial day (randomized).	
Reporting group title	Lumbar Ultrasound Trident (LUT)
Reporting group description:	
All included trial subjects received a lumbar plexus block with the LUT technique either on the first or the second trial day (randomized).	

Primary: Block procedure time

End point title	Block procedure time
End point description:	
End point type	Primary
End point timeframe:	
Assessed after pre-scanning from the time the ultrasound transducer was placed on the skin of the trial subject to the block needle was withdrawn after completed injection.	

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: second				
arithmetic mean (standard deviation)	238 (± 74)	334 (± 156)		

Statistical analyses

Statistical analysis title	Block procedure time
Statistical analysis description:	
Comparison of normal distributed difference between two paired continuous variabels.	
Comparison groups	Shamrock v Lumbar Ultrasound Trident (LUT)
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0089
Method	One-sample Student t test
Parameter estimate	Mean difference (final values)
Point estimate	-98

Confidence interval	
level	95 %
sides	2-sided
lower limit	-168
upper limit	-28

Notes:

[1] - Because this is a statistical test of paired variables, only the 19 subjects that completed both interventions were included in the comparative analysis.

Secondary: Number of block needle insertions

End point title	Number of block 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	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Number				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	6 (2 to 12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Block needle insertion point

End point title	Block needle insertion point

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 sagittal midline.

End point type	Secondary

End point timeframe:

Measured immediately after completed injection.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: cm				
median (inter-quartile range (Q1-Q3))	3 (3 to 3)	5 (5 to 6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Block needle depth

End point title	Block 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 after completed injection.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: cm				
median (inter-quartile range (Q1-Q3))	8 (7 to 8.5)	7 (6.5 to 7)		

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 triggering 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	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: mA				
median (inter-quartile range (Q1-Q3))	0.5 (0.32 to 0.7)	0.36 (0.32 to 0.46)		

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	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
Quadriceps femoris muscle response	17	13		
Sartorius muscle response	1	3		
Other muscular response	0	0		
Paresthesia	0	1		
None	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Discomfort during block procedure

End point title	Discomfort during block procedure

End point description:

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 type	Secondary

End point timeframe:

Assessed immediately after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: NRS 0-10				
median (full range (min-max))	3 (2 to 4)	4 (3 to 6)		

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	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: mmHg				
arithmetic mean (standard deviation)	1.1 (± 9.4)	-2.7 (± 11.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Perineural spread of local anaesthetics

End point title	Perineural spread of local anaesthetics

End point description:

Perineural spread of local anaesthetic was assessed as positive when visual contact between the local anaesthetic and the nerve on MRI was confirmed. Perineural spread was assessed for: anterior rami L1-S1; the femoral, the obturator, and the lateral femoral cutaneous nerves; and the lumbosacral trunk on the ipsilateral side as the block injection.

End point type	Secondary

End point timeframe:

Perineural spread of lidocaine was assessed on MRI scans sampled 15 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
Anteriur ramus L1	7	7		
Anterior ramus L2	19	15		
Anterior ramus L3	18	16		
Anterior ramus L4	15	12		
Anterior ramus L5	3	6		
Anterior ramus S1	0	1		
Femoral nerve	18	15		
Obturator nerve	14	14		
Lateral femoral cutaneous nerve	16	15		
Lumbosacral trunk	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Epidural spread of local anaesthetics

End point title	Epidural spread of local anaesthetics

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 anaesthetics was assessed on MRI sampled 15 minutes after completed intervention and during sensory mapping 45 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
Epidural spread	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Motor block

End point title	Motor block

End point description:

Motor block of the femoral nerve (knee extension), obturator nerve (hip adduction), superior gluteal nerve (hip abduction), and lumbosacral trunk (knee flexion), respectively, was assessed as present when the post-block muscle force of each motion was ≤ 50% of baseline muscle force.

End point type	Secondary

End point timeframe:

Baseline muscle force (mmHg) was assessed on the first trial day prior to intervention. Post-block muscle force (mmHg) was assessed 30 min after completed intervention on each trial day.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
Femoral nerve motor block	14	15		
Obturator nerve motor block	12	14		
Superior gluteal nerve motor block	3	5		
Lumbosacral trunk motor block	9	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory block - Cold

End point title	Sensory block - Cold

End point description:

Sensory block for cold in the dermatomes T8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for cold was absent.

End point type	Secondary

End point timeframe:

Assessed 45 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
T8	0	0		
T9	0	0		
T10	0	0		
T11	0	0		
T12	0	0		
L1	2	0		
L2	12	9		
L3	16	15		
L4	11	15		
L5	5	6		
S1	14	14		
S2	0	1		
S3	0	1		
Lateral femoral cutanous nerve	14	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory block - Warmth

End point title	Sensory block - Warmth

End point description:

Sensory block for warmth in the dermatomes T8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for warmth was absent.

End point type	Secondary

End point timeframe:

Assessed 45 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
T8	0	0		
T9	0	0		
T10	0	0		
T11	0	0		
T12	0	0		
L1	4	1		
L2	12	8		

L3	15	15		
L4	11	15		
L5	2	3		
S1	10	9		
S2	0	1		
S3	0	1		
Lateral femoral cutanous nerve	15	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory block - Touch

End point title	Sensory block - Touch

End point description:

Sensory block for touch in the dermatomes T8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for touch was absent.

End point type	Secondary

End point timeframe:

Assessed 45 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
T8	0	0		
T9	0	0		
T10	0	0		
T11	0	0		
T12	0	0		
L1	4	0		
L2	11	6		
L3	7	10		
L4	9	12		
L5	0	0		
S1	0	0		
S2	0	0		
S3	0	1		
Lateral femoral cutaneous nerve	16	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensory block - Pain

End point title	Sensory block - Pain

End point description:

Sensory block for pinprick (pain) in the dermatomes T8-S3 and in the skin area innervated by the lateral femoral cutaneous nerve, respectively, was assessed as present when the somatosensation for pinprick (pain) was absent.

End point type	Secondary

End point timeframe:

Assessed 45 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
T8	0	0		
T9	0	0		
T10	0	0		
T11	0	0		
T12	0	0		
L1	4	0		
L2	13	8		
L3	12	15		
L4	9	13		
L5	0	2		
S1	2	3		
S2	0	2		
S3	1	2		
Lateral femoral cutaneous nerve	13	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Block success

End point title	Block success

End point description:

Block success was assessed as motor block of the femoral and obturator nerves, and sensory block of the lateral femoral cutaneous nerve. Motor block is a proxy marker for sensory block and was assessed as successful when the post-block muscle strength of the femoral and obturator nerves, respectively, was ≤ 50% of baseline muscle force. Success of sensory block of the lateral femoral cutaneous nerve (LFCN) was assessed as present when the sensory for cold and/or pinprick (pain) was absent.

End point type	Secondary

End point timeframe:

Motor block of the femoral and obturator nerves was assessed at 30 min after completed injection.

Sensor block of cold and/or pinprick of the lateral femoral cutaneous nerve was assessed at 45 min after completed injection.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: Subjects				
Block success of femoral and obturator nerves	12	14		
Block success of femoral, obturator, and LCFN	7	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) of plasma lidocaine (p-lidocaine)

End point title	Maximum concentration (Cmax) of plasma lidocaine (p-lidocaine)

End point description:

End point type	Secondary

End point timeframe:

Cmax of p-lidocaine was assessed in blood sampled at 0, 5, 10, 20, 40, 60, and 90 minutes after intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: µg*ml-1				
arithmetic mean (standard deviation)	1.45 (± 0.35)	1.4 (± 0.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax p-lidocaine

End point title	Time to Cmax p-lidocaine

End point description:

End point type	Secondary

End point timeframe:

Time to Cmax was estimated in the period 0-90 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: minutes				
median (inter-quartile range (Q1-Q3))	60 (60 to 60)	60 (40 to 60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lidocaine concentration-area under the curve

End point title	Lidocaine concentration-area under the curve

End point description:

End point type	Secondary

End point timeframe:

Assessed in the period 0-90 minutes after completed intervention.

End point values	Shamrock	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: µg*min*ml-1				
arithmetic mean (standard deviation)	102 (± 25)	102 (± 27)		

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 Shamrock vs. the LUT 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	Lumbar Ultrasound Trident (LUT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: USD				
number (not applicable)	0	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Continuous assessment of adverse events from the start of pre-scanning until the discharge after intervention on the trial day. All trial subjects were urged to self-report any adverse events after discharge.

Adverse event reporting additional description:

Regular assessment of adverse events from the start of pre-scanning until the end of observation. All trial subjects were systematically asked about any adverse events by the time of discharge. All trial subjects were urged to self-report any adverse events after discharge - both between the trial days and after the last trial day.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Shamrock lumbar plexus block
Reporting group description: -	
Reporting group title	Lumbar Ultrasound Trident lumbar plexus block

Reporting group description: -

Serious adverse events	Shamrock lumbar plexus block	Lumbar Ultrasound Trident lumbar plexus block	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Shamrock lumbar plexus block	Lumbar Ultrasound Trident lumbar plexus block	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	
Vascular disorders			
Phlebitis superficial	Additional description: Superficial phlebitis on the site of the i.v. access used for blood sampling.		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Palpitations	Additional description: Short and temporary sensation of palpitations related to injection of lidocaine-adrenaline.		
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash	Additional description: Skin rash where plaster had been used to fix i.v. access used for blood sampling and sterile surgical cover, respectively.		
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	
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