Clinical trial results:
A Single-Blind Randomised Controlled Pilot trial of Corticosteroid Injection for Shoulder Pain

Summary

EudraCT number	2012-000147-27
Trial protocol	GB
Global end of trial date	31 March 2013

Results information

Result version number	v1 (current)
This version publication date	14 May 2016
First version publication date	14 May 2016
Summary attachment (see zip file)	Final analysis published article (RCT2 Holt T (Trials 2013).pdf)

Trial information

Trial identification

Sponsor protocol code	TH/RCT2/0001

Additional study identifiers

ISRCTN number	ISRCTN82357435
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Block 60, Churchill Hospital, Oxford, United Kingdom, OX3 7LJ
Public contact	Dr Tim Holt, Nuffield Department of Primary Care Health Sciences University of Oxford, tim.holt@phc.ox.ac.uk
Scientific contact	Dr Tim Holt, Nuffield Department of Primary Care Health Sciences University of Oxford, tim.holt@phc.ox.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	31 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2013
Global end of trial reached?	Yes
Global end of trial date	31 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To measure feasibility issues including rates of recruitment and loss to follow up, including withdrawal from a randomised trial of a corticosteroid shoulder injection in patients with rotator cuff tendinopathy or adhesive capsulitis.

Protection of trial subjects:

Risk assessment took place on 22/6/2016 to identify potential risks associated with the trial and IMP. Prior to recruitment of participants, trial GPs underwent study specific training in the assessment of shoulder pain, including the distinction of rotator cuff tendinopathy from adhesive capsulitis and the distinction of these two conditions and other disorders not relevant to this study. They also received training on the injection technique into the subacromial space employed in this trial. Training was led by an academic orthopedic shoulder surgeon from the Nuffield Orthopaedic Centre at Oxford and is based on the British Elbow and Shoulder Society (BESS) Pathway Guideline for Sub-acromial Pain. The trial GPs also received study specific good clinical practice (GCP) training and training in the study procedures (for example, case report form (CRF) completion, safety reporting) from the Primary Care Clinical Trials Unit. The training took less than 1 day to complete.

Background therapy:

The vials were sourced and labeled by Almac Clinical Services Ltd (Almac House, 20 Seagoe Industrial Estate, Craigavon, BT63 5QD, UK) and stored according to the manufactures specifications in the general practice premises.

Evidence for comparator:

Lidocaine is a medicine which is used in neuropathic pain.

Actual start date of recruitment	01 September 2012
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	United Kingdom: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	30
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 20/9/2012 and 27/2/2013 from 6 GP practices within the Oxforshire (UK) region

Pre-assignment

Screening details:

Forty nine people were screened for eligibiity. Nine were excluded due to not eligible (n=7) and declined to participate (n=2)

Period 1

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

Blinding implementation details:

The trial injection was administered by the GP without disclosing to the participant which treatment they were receiving.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group M

Arm description:

methylprednisolone acetate 40 mg with lidocaine 1% in 1 ml

Arm type	Experimental
Investigational medicinal product name	methylprednisolone acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Periarticular use

Dosage and administration details:

Total dose = 40mg (1 single injection)

Arm title	Group L

Arm description:

lidocaine 1% in 1 ml alone

Arm type	Active comparator
Investigational medicinal product name	lidocaine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Periarticular use

Dosage and administration details:

Total dose = 20mg (1 single injection)

Number of subjects in period 1	Group M	Group L
Started	19	21
Completed	19	21

Baseline characteristics

Reporting groups

Reporting group title	Group M
Reporting group description:	
methylprednisolone acetate 40 mg with lidocaine 1% in 1 ml	
Reporting group title	Group L
Reporting group description:	
lidocaine 1% in 1 ml alone	

Reporting group values	Group M	Group L	Total
Number of subjects	19	21	40
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	61.5	56	
standard deviation	± 5.8	± 11.3	-
Gender categorical			
Units: Subjects			
Female	11	15	26
Male	8	6	14
Which shoulder is affected			
Units: Subjects			
Right	13	12	25
Left	6	9	15

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised irrespective of whether the participants received any trial medication	

Reporting group values	ITT		
Number of subjects	40		

Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	58.6		
standard deviation	± 9.4		
Gender categorical Units: Subjects			
Female	26		
Male	14		
Which shoulder is affected Units: Subjects			
Right	25		
Left	15		

End points

End points reporting groups

Reporting group title	Group M
Reporting group description:	
methylprednisolone acetate 40 mg with lidocaine 1% in 1 ml	
Reporting group title	Group L
Reporting group description:	
lidocaine 1% in 1 ml alone	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised irrespective of whether the participants received any trial medication	

Primary: Attrition rate at 2 weeks

End point title	Attrition rate at 2 weeks
End point description:	
Number of questionnaires not returned	
End point type	Primary
End point timeframe:	
2 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: subjects				
Yes	0	0		
No	19	21		

Statistical analyses

Statistical analysis title	Attrition rate - no formal analysis
Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	> 999 [2]
Method	N/A

Notes:

[1] - This is a pilot study and therefore no formal statistical analysis was performed as stated in the statistical analysis plan

[2] - This P-value is N/A because there was no formal statistical comparison for this outcome because it's a pilot study

Primary: Compliance

End point title	Compliance

End point description:

Number adhered to the allocated treatment

End point type	Primary

End point timeframe:

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: subjects				
Adhered	18	18		

Statistical analyses

Statistical analysis title	Compliance

Statistical analysis description:

Compliance with the allocated treatment

Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.607
Method	Fisher exact

Primary: Attrition rate at 4 weeks

End point title	Attrition rate at 4 weeks

End point description:

Number of questionnaires not returned

End point type	Primary

End point timeframe:

4 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	0	1		
No	19	20		

Statistical analyses

Statistical analysis title	Attrition rate - no formal analysis
Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 999 [4]
Method	N/A

Notes:

[3] - This is a pilot study and therefore no formal statistical analysis was performed as stated in the statistical analysis plan

[4] - This P-value is N/A because there was no formal statistical comparison for this outcome because it's a pilot study

Primary: Attrition rate at 12 weeks

End point title	Attrition rate at 12 weeks
End point description:	
Number of questionnaire not returned	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	0	2		
No	19	19		

Statistical analyses

Statistical analysis title	Attrition rate - no formal analysis
Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 999 [6]
Method	N/A

Notes:

[5] - This is a pilot study and therefore no formal statistical analysis was performed as stated in the statistical analysis plan

[6] - This P-value is N/A because there was no formal statistical comparison for this outcome because it's a pilot study

Secondary: Change in OSS at 4 weeks

End point title	Change in OSS at 4 weeks
End point description:	
Oxford shoulder score	
End point type	Secondary
End point timeframe:	
4 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: point				
arithmetic mean (standard deviation)	3.9 (± 8.5)	6.3 (± 10.1)		

Statistical analyses

Statistical analysis title	Change at 4 weeks from baseline
Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (net)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	3.4

Secondary: Change in OSS at 12 weeks

End point title	Change in OSS at 12 weeks
End point description:	
Change in Oxford Shoulder Score from baseline	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: points				
arithmetic mean (standard deviation)	4.2 (± 9.1)	8.2 (± 11.3)		

Statistical analyses

Statistical analysis title	Change in OSS at 12 weeks from baseline
Comparison groups	Group M v Group L
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (net)
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	3.2

Secondary: Patient's satisfaction - problem with shoulder now? at 2 weeks

End point title	Patient's satisfaction - problem with shoulder now? at 2 weeks
End point description:	
End point type	Secondary
End point timeframe:	
2 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Much worse	1	2		
Slightly worse	3	7		
No change	3	5		
Slightly better	10	4		
Much better	1	2		
No problem at all	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction - problem with shoulder now? at 4 weeks

End point title	Patient's satisfaction - problem with shoulder now? at 4 weeks
End point description:	
End point type	Secondary
End point timeframe:	
4 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Number of participants				
Much worse	2	1		
Slightly worse	1	2		
No change	6	7		
Slightly better	4	5		
Much better	5	3		
No problem at all	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction - problem with shoulder now? at 12 weeks

End point title	Patient's satisfaction - problem with shoulder now? at 12 weeks
End point description:	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Number of participants				
Much worse	0	0		
Slightly worse	2	4		
No change	8	3		
Slightly better	3	3		
Much better	5	8		
No problem at all	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction with injection - how pleased? 2 weeks

End point title	Patient's satisfaction with injection - how pleased? 2 weeks
End point description:	
End point type	Secondary
End point timeframe:	
2 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Very disappointed	4	7		
Not very pleased	5	9		
Fairly pleased	9	3		
Very pleased	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction with injection - how pleased? 4 weeks

End point title	Patient's satisfaction with injection - how pleased? 4 weeks
End point description:	
End point type	Secondary
End point timeframe:	
4 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: Number of participants				
Very disappointed	6	7		
Not very pleased	3	6		
Fairly pleased	4	4		
Very pleased	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction with injection - how pleased? 12 weeks

End point title	Patient's satisfaction with injection - how pleased? 12 weeks
End point description:	

End point type	Secondary
End point timeframe:	

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Number of participants				
Very disappointed	8	5		
Not very pleased	2	5		
Fairly pleased	5	5		
Very pleased	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction - still choose the injection? 2 weeks

End point title	Patient's satisfaction - still choose the injection? 2 weeks
End point description:	

End point type	Secondary

End point timeframe:

2 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
No	3	7		
Yes	14	10		
Not sure	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction - still choose the injection? 4 weeks

End point title	Patient's satisfaction - still choose the injection? 4 weeks
End point description:	

End point type	Secondary

End point timeframe:

4 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Number of participants				
No	1	4		
Yes	14	11		
Not sure	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's satisfaction - still choose the injection? 12 weeks

End point title	Patient's satisfaction - still choose the injection? 12 weeks
End point description:	

End point type	Secondary

End point timeframe:

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Number of participants				
No	4	4		
Yes	12	10		
Not sure	3	5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - Pain killers: 2 weeks

End point title	Received other treatment - Pain killers: 2 weeks
End point description:	

End point type	Other pre-specified

End point timeframe:

2 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	21		
Units: Number of participants				
Yes	8	11		
No	10	4		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - Pain killers: 4 weeks

End point title	Received other treatment - Pain killers: 4 weeks
End point description:	

End point type	Other pre-specified

End point timeframe:

4 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Number of participants				
Yes	7	11		
No	12	9		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - Pain killers: 12 weeks

End point title	Received other treatment - Pain killers: 12 weeks
End point description:	

End point type	Other pre-specified
End point timeframe:	

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: Number of participants				
Yes	7	11		
No	10	8		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - anti-infammatory medication: 2 weeks

End point title	Received other treatment - anti-infammatory medication: 2 weeks
End point description:	

End point type	Other pre-specified

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Number of participants				
Yes	5	10		
No	13	10		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - anti-infammatory medication: 4 weeks

End point title	Received other treatment - anti-infammatory medication: 4 weeks
End point description:	

End point type	Other pre-specified
End point timeframe:	
4 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: Number of participants				
Yes	4	7		
No	13	12		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - anti-infammatory medication: 12 weeks

End point title	Received other treatment - anti-infammatory medication: 12 weeks
End point description:	

End point type	Other pre-specified

End point timeframe:

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	16		
Units: Number of participants				
Yes	6	10		
No	13	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - physiotherapy: 2 weeks

End point title	Received other treatment - physiotherapy: 2 weeks

End point description:

End point type	Other pre-specified

End point timeframe:

2 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: Number of participants				
Yes	0	1		
No	17	19		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - physiotherapy: 4 weeks

End point title	Received other treatment - physiotherapy: 4 weeks

End point description:

End point type	Other pre-specified

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	19		
Units: Number of participants				
Yes	1	3		
No	15	16		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received other treatment - physiotherapy: 12 weeks

End point title	Received other treatment - physiotherapy: 12 weeks
End point description:	

End point type	Other pre-specified
End point timeframe:	

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: Number of participants				
Yes	1	6		
No	17	12		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received rescue steroid injection

End point title	Received rescue steroid injection
End point description:	

End point type	Other pre-specified
End point timeframe:	

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	1	3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received physiotherapy in 12 weeks

End point title	Received physiotherapy in 12 weeks

End point description:

End point type	Other pre-specified

End point timeframe:

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	3	3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received prescribed analgesia in 12 weeks

End point title	Received prescribed analgesia in 12 weeks

End point description:

End point type	Other pre-specified

End point timeframe:

12 weeks

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	2	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Received NSAID in 12 weeks

End point title	Received NSAID in 12 weeks
End point description:	

End point type	Other pre-specified
End point timeframe:	
12 weeks	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	1	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Treatment allocation blinding assessment

End point title	Treatment allocation blinding assessment
End point description:	

End point type	Other pre-specified
End point timeframe:	
At the time of injection	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
100%	13	15		
89-99%	6	6		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Serious adverse event

End point title	Serious adverse event
End point description:	

End point type	Other pre-specified
End point timeframe:	
Throughout the trial	

End point values	Group M	Group L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Number of participants				
Yes	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events reporting occurs through the entire duration of the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Frequency threshold for reporting non-serious adverse events: 0 %

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: Both methylprednisolone acetate and lidocaine hydrochloride are commonly used medications in a primary care setting, have well defined safety profiles and are being used for authorised indications. As a result of this no non-serious adverse events will be recorded in this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2012	Substantial amendment with regards to putting up posters in the waiting rooms of the GP surgeries that are participating in the trial. The posters will ask patients if they have shoulder pain and if they match certain requirements of the inclusion criteria. The patients will be asked the speak with the trial GP at the practice for further information. In addition, to have patient leaflets in the reception areas of the GP surgeries. The leaflets will detail information about the trial and will ask the patient to contact the trial GP at the practice for further information. It is anticipated that these documents will help aid the practices in recruiting participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported