



## Clinical trial results:

### Systemic versus ultrasound-guided local glucocorticoid treatment, among rheumatoid arthritis patients with tenosynovitis - a randomized double blind study

#### Summary

EudraCT number	2013-003486-34
Trial protocol	DK
Global end of trial date	22 December 2016

#### Results information

Result version number	v1 (current)
This version publication date	30 August 2017
First version publication date	30 August 2017
Summary attachment (see zip file)	Intramuscular versus ultrasound guided peritendinous glucocorticoid injection for tenosynovitis in patients with rheumatoid arthritis - A randomised, double-blind, controlled study (ACR_sultan_final.docx)

#### Trial information

##### Trial identification

Sponsor protocol code	39132
-----------------------	-------

##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Mikkel Østergaard
Sponsor organisation address	Valdemar Hansens Vej 13 Rød opgang 5, stuen, Glostrup, Denmark, 2600
Public contact	Mads Ammitzbøll Danielsen, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, mo@dadlnet.dk
Scientific contact	Mads Ammitzbøll Danielsen, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, mo@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	23 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2015
Global end of trial reached?	Yes
Global end of trial date	22 December 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Explore whether ultrasound-guided glucocorticoid injection in the synovial sheath has better effect than intramuscularly glucocorticoid injection among patients with tenosynovitis, assessed by US examination, pain VAS-score and clinical evaluation.

Protection of trial subjects:

US assessment

Clinical assessment

A patient reported visual analogue scale (0-100 mm) for tenosynovitis pain (VAS TS)

Disease Activity Score for 28 joints (DAS28), using C-reactive protein (CRP)

Patient global visual analogue scale (VAS Global)

Health Assessment Questionnaire (HAQ)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

Notes:

<b>Subjects enrolled per age group</b>	
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)	39
From 65 to 84 years	11
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

All patients were recruited from the rheumatology outpatient clinic at Rigshospitalet, Denmark, from December 2013 to September 2015 by study independent physicians. All recruited patients were screened, i.e. clinical and US examinations were performed of the above mentioned selected tendon sheaths, by the study investigators

### Pre-assignment

Screening details:

Patients were screened with a clinical and US examinations of the selected tendon sheaths

### Pre-assignment period milestones<sup>[1]</sup>

Number of subjects started	50
Intermediate milestone: Number of subjects	2 weeks: 49
Intermediate milestone: Number of subjects	4 weeks: 48
Intermediate milestone: Number of subjects	12: 33
Number of subjects completed	50

Notes:

[1] - The number of subjects at the milestone is less than the number that completed the pre-assignment period. It is expected the number of subjects at the milestones will be greater than, or equal to the number that completed the pre-assignment period.

Justification: It is the same problem as the first one.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
Arm title	A"im group"

Arm description:

RA patients with TS were randomised into two double-blind groups. An "im group" receiving im injection of 14 milligrams (2 ml) of betamethasone dinatriumphosphate (BM) (e.g. glucocorticoid) in the gluteal muscles and US guided isotonic saline injection in up to two tendon sheaths (maximum 1 ml for each tendon sheath)

Arm type	Active comparator
Investigational medicinal product name	Betamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

14 milligrams (2 ml) of betamethasone

Arm title	B; "intratenosynovial group"
-----------	------------------------------

Arm description:

A"intratenosynovial group" receiving 2 ml of im isotonic saline and US guided BM injection in up to two tendon sheaths (maximum 7 milligrams (1 ml) for each tendon sheath). Follow up was undertaken at 2,

4 and 12 weeks (+/- 3 days) after injections.

Arm type	Active comparator
Investigational medicinal product name	Betamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intraarticular use

Dosage and administration details:

7 milligrams (1 ml) of betamethasone intratenosynovial

<b>Number of subjects in period 1</b>	A"im group"	B; "intratenosynovial group"
Started	25	25
2 weeks	23 <sup>[2]</sup>	25
4 weeks	23 <sup>[3]</sup>	25
12 weeks	15 <sup>[4]</sup>	18 <sup>[5]</sup>
Baseline	25	25
Completed	25	25

Notes:

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: It is the same problem as the first one.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The calculated in the program, keep saying that 25 minus 7 is not 18. So I have entered 25 at start and 25 completed. It is the same for the rest.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: It is the same problem as the first one.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: It is the same problem as the first one.

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	A"im group"
Reporting group description: RA patients with TS were randomised into two double-blind groups. An "im group" receiving im injection of 14 milligrams (2 ml) of betamethasone dinatriumphosphate (BM) (e.g. glucocorticoid) in the gluteal muscles and US guided isotonic saline injection in up to two tendon sheaths (maximum 1 ml for each tendon sheath)	
Reporting group title	B; "intratenosynovial group"
Reporting group description: A"intratenosynovial group" receiving 2 ml of im isotonic saline and US guided BM injection in up to two tendon sheaths (maximum 7 milligrams (1 ml) for each tendon sheath). Follow up was undertaken at 2, 4 and 12 weeks (+/- 3 days) after injections.	

### Primary: Primary end point

End point title	Primary end point
End point description: The primary outcome was the proportion of subjects in each group achieving US TS remission, defined as US TS GS score $\leq 1$ and Doppler score = 0, at week 4.	
End point type	Primary
End point timeframe: 4 weeks	

End point values	A"im group"	B; "intratenosynovial group"		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: numbers	6	16		

### Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	A"im group" v B; "intratenosynovial group"
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence <sup>[1]</sup>
P-value	> 0.05 <sup>[2]</sup>
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	48

Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	95
Variability estimate	Standard error of the mean

Notes:

[1] - Binary data (including the primary outcome) were analysed by Fisher's exact test, and relative risks were calculated between the groups at 2, 4 and 12 weeks. The 95% confidence interval (CI) for the difference was computed by the Agresti-Caffo method. A non-responder imputation (NRI) was used for missing data in these analyses.

[2] - Fisher's exact test



## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

To the last visit (December 2016)

Assessment type	Non-systematic
-----------------	----------------

### Dictionary used

Dictionary name	SNOMED CT
-----------------	-----------

Dictionary version	1
--------------------	---

### Reporting groups

Reporting group title	Sultan; Both arms
-----------------------	-------------------

Reporting group description: -

Serious adverse events	Sultan; Both arms		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Sultan; Both arms		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		

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: There was no adverse Events due to protocol definitions

## **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