Clinical trial results:
Treatment of rotator cuff syndrome and bursitis: A double blind, controlled trial to assess the efficacy and safety of Traumeel® S injection versus corticosteroid injections and versus placebo TRARO (Traumeel® S in Rotator Cuff Syndrome)-Study

Summary

EudraCT number	2012-003393-12
Trial protocol	DE BE ES
Global end of trial date	24 June 2014

Results information

Result version number	v1 (current)
This version publication date	15 June 2016
First version publication date	15 June 2016

Trial information

Trial identification

Sponsor protocol code	TRARO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01702233
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biologische Heilmittel Heel GmbH
Sponsor organisation address	Dr. Reckeweg-Str. 2-4, Baden-Baden, Germany, 76532
Public contact	Dr. Istvan Zatik, Biologische Heilmittel Heel GmbH, +49 7221-5010, info@heel.com
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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	24 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2014
Global end of trial reached?	Yes
Global end of trial date	24 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of subjective parameters in patients with rotator cuff syndrome and bursitis by visual analogue scale (VAS).

Protection of trial subjects:

Standard protection of trial subjects according to ICH GCP requirements was applied.

Background therapy:

Paracetamol (500 mg PRN) was permitted during the study as rescue medication for pain relief with a maximal daily dose of 2000 mg. No Paracetamol intake was allowed within 24 hours before any efficacy measures.

Evidence for comparator:

Periarticular injection of dexamethasone is the established medication for treatment of shoulder conditions such as rotator cuff syndrome and Bursitis.

Actual start date of recruitment	16 April 2013
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	Spain: 38
Country: Number of subjects enrolled	Germany: 129
Country: Number of subjects enrolled	Belgium: 9
Worldwide total number of subjects	176
EEA total number of subjects	176

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)	172
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was carried out in 10 sites in Europe: 2 sites in Belgium, 4 in Germany and 4 in Spain. The recruitment phase was completed when patients were enrolled, and the planned duration of recruitment period was about 12 months. Enrolment started in April 2013; the last Patient was enroled in February 2014 to the study. LPLV was on 24 June 2014

Pre-assignment

Screening details:

Observations/procedures performed and checked included check of inclusion/exclusion criteria, completion of physical examination and medical history, bilateral shoulder examination, VAS measurement, bilateral examination of ROM, Jobe/Painful Arc tests and DASH score, dispensation of 500 mg paracetamol as rescue medication for pain relief etc.

Period 1

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

Blinding implementation details:

Patients were randomly allocated to Traumeel® S, dexamethasone, or placebo in a 2:2:1 randomization. The randomization was stratified by site. The patients were randomized in ascending order of the site-specific randomization list.

Arms

Are arms mutually exclusive?	Yes
Arm title	Traumeel Safety Group

Arm description:

72 subjects received 2ml Traumeel once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Arm type	Experimental
Investigational medicinal product name	Traumeel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Periarticular use

Dosage and administration details:

One ampoule of 2 ml Traumeel contains:
Calendula officinalis, 2 mg, (Dil. D2)
Atropa Belladonna, 2 mg, (Dil. D2)
Aconitum napellus, 1.2 mg, (Dil. D2)
Bellis perennis, 1mg, (Dil. D2)
Hypericum perforatum, 0.6 mg, (Dil. D2)
Echinacea, 0.5 mg, (Dil. D2)
Echinacea purpurea, 0.5 mg, (Dil. D2)
Symphytum officinale 2 mg (Dil. D6)
Matricaria recutita, 2 mg, (Dil. D3)
Achillea millefolium, 2 mg, (Dil. D3)
Mercurius solubilis Hahnemanni, 1 mg, (Dil. D6)
Hepar sulfuris, 2 mg, (Dil. D6)
Hamamelis virginiana 0.2 mg, (Dil. D1)
Arnica montana, 2 mg, (Dil. D2)
Route of administration: periarticular use
Total administered: 6 ml (2 ml/week for 3 weeks)

Arm title	Fortecortin Safety Group

Arm description:

67 participants were randomized to Fortecortin. The subjects received 2ml Fortecortin once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Arm type	Active comparator
Investigational medicinal product name	Fortecortin (dexamethasone)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Periarticular use

Dosage and administration details:

One vial of 2 ml Fortecortin contains 8 mg dexamethasone.
Route of administration: periarticular use
Total administered: 6 ml (2 ml/week for 3 weeks), i.e. 48 mg dexamethasone

Arm title	Placebo Safety Group

Arm description:

36 participants were randomized to placebo. The subjects received 2ml placebo once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Periarticular use

Dosage and administration details:

One ampoule of 2 ml placebo containing sodium chloride and water for injections, was administered once per week for 3 weeks.

Number of subjects in period 1[1]	Traumeel Safety Group	Fortecortin Safety Group	Placebo Safety Group
Started	72	67	36
Completed	67	64	31
Not completed	5	3	5
Consent withdrawn by subject	1	-	-
Physician decision	2	-	-
Adverse event, non-fatal	-	2	2
private problems, broken ampoules	-	-	2
Lack of efficacy	2	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 176 subjects were randomized, 1 subject (Traumeel S group) was not treated. Thus, 175 of the randomized patients were included in the Safety Set, 72 patients in the Traumeel S group, 67 patients in the Fortecortin group and 36 patients in the Placebo group. The Safety Analysis Set was used

for all analyses of safety, tolerability, and background characteristics.

Baseline characteristics

Reporting groups	
Reporting group title	Traumeel Safety Group

Reporting group description:

72 subjects received 2ml Traumeel once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Reporting group title	Fortecortin Safety Group

Reporting group description:

67 participants were randomized to Fortecortin. The subjects received 2ml Fortecortin once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Reporting group title	Placebo Safety Group

Reporting group description:

36 participants were randomized to placebo. The subjects received 2ml placebo once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Reporting group values	Traumeel Safety Group	Fortecortin Safety Group	Placebo Safety Group
Number of subjects	72	67	36
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	69	66	36
From 65-84 years	3	1	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51	51.9	51.8
standard deviation	± 6.9	± 7.02	± 6.74
Gender categorical Units: Subjects			
Female	41	37	20
Male	31	30	16
Ethnic group Units: Subjects			
White	71	66	35
Black	1	0	0
Asian	0	0	0
Other	0	1	1

Height			
Units: cm			
arithmetic mean	171.3	170.6	169.9
standard deviation	± 10.24	± 8.01	± 11.32
Weight			
Units: kg			
arithmetic mean	76.4	79.2	78.8
standard deviation	± 16.57	± 14.9	± 16.9
BMI			
Units: kg/m2			
arithmetic mean	25.92	27.29	27.14
standard deviation	± 4.455	± 5.455	± 4.382

Reporting group values	Total		
Number of subjects	175		
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)	171		
From 65-84 years	4		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	98		
Male	77		
Ethnic group			
Units: Subjects			
White	172		
Black	1		
Asian	0		
Other	2		
Height			
Units: cm			
arithmetic mean			
standard deviation	-		
Weight			
Units: kg			
arithmetic mean			
standard deviation	-		
BMI			
Units: kg/m2			

arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Traumeel Safety Group

Reporting group description:

72 subjects received 2ml Traumeel once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Reporting group title	Fortecortin Safety Group

Reporting group description:

67 participants were randomized to Fortecortin. The subjects received 2ml Fortecortin once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Reporting group title	Placebo Safety Group

Reporting group description:

36 participants were randomized to placebo. The subjects received 2ml placebo once a week for 3 continuous weeks, using ultrasound-guided subacromial periarticular injection. Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and Background characteristics.

Subject analysis set title	Traumeel S Per-Protocol Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the Full Analysis Set (subset of the Safety Analysis Set) without major protocol deviations formed the Per-Protocol Set. The PP Set was used as the primary population for the analysis of efficacy.

Subject analysis set title	Fortecortin Per-Protocol Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the Full Analysis Set (subset of the Safety Analysis Set) without major protocol deviations formed the Per-Protocol Set. The PP Set was used as the primary population for the analysis of efficacy.

Subject analysis set title	Placebo Per-Protocol Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients in the Full Analysis Set (subset of the Safety Analysis Set) without major protocol deviations formed the Per-Protocol Set. The PP Set was used as the primary population for the analysis of efficacy.

Primary: Abduction rotation pain VAS for active external rotation at day 22 (Traumeel vs Fortecortin)

End point title	Abduction rotation pain VAS for active external rotation at day 22 (Traumeel vs Fortecortin)

End point description:

Primary Efficacy Variable was the change from baseline in VAS for abduction rotation pain at Visit 5 (Day 22) (Traumeel S injections versus corticoid injections) for active external rotation.

End point type	Primary

End point timeframe:

Screening (max. -7 days, visit 1), Day 1 Baseline (visit 2) Day 22 ± 1 day (visit 5)

End point values	Traumeel S Per-Protocol Set	Fortecortin Per-Protocol Set	Placebo Per-Protocol Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	58	58	27	
Units: mm				
arithmetic mean (standard deviation)				
Baseline	58.2 (± 19.76)	61 (± 17.87)	55.6 (± 18.43)	
Visit 5	39.5 (± 25.2)	33.8 (± 26.17)	38.5 (± 24.49)	
Change from baseline	-18.7 (± 21.49)	-27.2 (± 23.44)	-17.1 (± 23.94)	

Statistical analyses

Statistical analysis title	Analysis of primary endpoint

Statistical analysis description:

A one-sided test of non-inferiority of Traumeel® S with respect to dexamethasone at Level 0.025 was computed using an analysis of covariance (ANCOVA) model with treatment group and centre as qualitative factors and the baseline value of the abduction rotation pain VAS for active external rotation as a covariate.

Comparison groups	Fortecortin Per-Protocol Set v Traumeel S Per-Protocol Set
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	ANCOVA
Parameter estimate	least squares mean difference
Point estimate	7.62
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	15.74
Variability estimate	Standard deviation
Dispersion value	4.11

Notes:

[1] - The test decision was based on a one-sided 97.5% confidence interval for the corresponding Treatment difference. The non-inferiority margin was set to 13 mm on a 0 - 100 mm VAS scale.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening (max. -7 days), Baseline, Day 1, Day 8 ± 1 day, Day 15 ± 1 day, Day 22 ± 1 day, Week 9 ± 3 days, Week 15 ± 3 days

Adverse event reporting additional description:

All AEs, occurred after the patient signed the IC were collected and reported on eCRF, regardless of whether they were reported by the patient, elicited by investigator questioning, detected through physical examination, or by other means. 86/175 treated patients (49%) reported 197 (s)AEs. 78 patients reported 171 TEAEs after 1st IMP Administration

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Traumeel Safety Group

Reporting group description:

Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and background characteristics.

Reporting group title	Fortecortin Safety Group

Reporting group description:

Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and background characteristics.

Reporting group title	Placebo Safety Group

Reporting group description:

Randomized patients who received at least one injection of study medication form the Safety Analysis Set. The Safety Analysis Set was used for all analyses of safety, tolerability, and background characteristics.

Serious adverse events	Traumeel Safety Group	Fortecortin Safety Group	Placebo Safety Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
auricular (atrial) fibrillation	Additional description: The SAE was severe and led to discontinuation of study drug after the first injection, the patient recovered. SAE was considered as „unrelated" due to delayed occurrence following 1st injection and due to pre-existing disease.		
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Traumeel Safety Group	Fortecortin Safety Group	Placebo Safety Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 72 (45.83%)	29 / 67 (43.28%)	16 / 36 (44.44%)
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Dental implantation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
injection site haematoma			
subjects affected / exposed	2 / 72 (2.78%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	2	1	0
Injection site joint effusion			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 72 (1.39%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Immune system disorders			
hypersensitivity			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0

seasonal allergy			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 72 (1.39%)	3 / 67 (4.48%)	2 / 36 (5.56%)
occurrences (all)	1	3	2
Pleurisy			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Loss of libido			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	1 / 72 (1.39%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	2 / 72 (2.78%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Ligament sprain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	3 / 72 (4.17%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	3	0	1
Formication			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	12 / 72 (16.67%)	11 / 67 (16.42%)	3 / 36 (8.33%)
occurrences (all)	12	11	3
Hypertonia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Intercostal neuralgia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 72 (0.00%)	2 / 67 (2.99%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Eye disorders			

Lacrimation increased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 72 (0.00%)	2 / 67 (2.99%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 72 (1.39%)	1 / 67 (1.49%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Back pain			
subjects affected / exposed	3 / 72 (4.17%)	1 / 67 (1.49%)	3 / 36 (8.33%)
occurrences (all)	3	1	3
Foot deformity			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Gouty arthritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	2 / 72 (2.78%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0

Neck pain			
subjects affected / exposed	4 / 72 (5.56%)	2 / 67 (2.99%)	2 / 36 (5.56%)
occurrences (all)	4	2	2
Pain in extremity			
subjects affected / exposed	1 / 72 (1.39%)	2 / 67 (2.99%)	1 / 36 (2.78%)
occurrences (all)	1	2	1
Periarthritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
bronchitis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 67 (1.49%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Influenza			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Lice infestation			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 72 (2.78%)	2 / 67 (2.99%)	0 / 36 (0.00%)
occurrences (all)	2	2	0
Oral herpes			
subjects affected / exposed	0 / 72 (0.00%)	0 / 67 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Periodontitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 67 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 67 (1.49%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			

subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0	1 / 67 (1.49%) 1	0 / 36 (0.00%) 0
Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all)	1 / 72 (1.39%) 1	0 / 67 (0.00%) 0	0 / 36 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2014	1. The number of patients to be enrolled was to be increased to 175 (instead of 160) patients to achieve a sufficient number of evaluable patients: Patients were not eligible for the per protocol analysis for the following reasons: a. methodology issues with performing the VAS as per protocol. A total of 11 patients was inadvertently instructed to perfom the VAS scoring differently from protocol, one patient performed the VAS scoring on one form for all visits and the visit could not be referenced thereafter and in one patient the VAS was not performed adequately at baseline. b. There were some drop-outs for the following reasons: Patients do not meet inclusion criteria (calcifications), in one case the patient was employed at site and in one case the random code was found open.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/15593187

http://www.ncbi.nlm.nih.gov/pubmed/8326275

http://www.ncbi.nlm.nih.gov/pubmed/10839557

http://www.ncbi.nlm.nih.gov/pubmed/17720798