Clinical trial results:
An open label, single dose phase Ib/IIa study to determine the safety and clinical effects of intra-articular injections of low doses of Lopain (MTX-071) in patients with chronic osteoarthritic knee joint pain

Summary

EudraCT number	2017-004049-26
Trial protocol	BE
Global end of trial date	16 August 2019

Results information

Result version number	v1 (current)
This version publication date	09 May 2021
First version publication date	09 May 2021

Trial information

Trial identification

Sponsor protocol code	MTX-071-P02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Mestex AG
Sponsor organisation address	Klosterberg 11, Basel, Switzerland, CH-4051
Public contact	Grünenthal Trial Information Desk, Mestex AG, Clinical-Trials@grunenthal.com
Scientific contact	Grünenthal Trial Information Desk, Mestex AG, Clinical-Trials@grunenthal.com

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	01 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the safety and tolerability of intra-articular injections of low doses of MTX-071 based on the incidence, nature and severity of AES /SAEs potentially causally related with the study medication.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization (ICH) Note for Guidance on Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP]/ICH/135/95) and with applicable local requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 December 2017
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	Belgium: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	21
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at two orthopedic clinics experienced in the treatment of osteoarthritis of the knee.

Pre-assignment

Screening details:

24 subjects were enrolled

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MTX-071 Group 1 - lido

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (5 ml lidocaine 2%, IA) premedication 15 minutes before MTX-071 IA administration single dose

Arm title	MTX-071 Group 2 - lido

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (5 ml lidocaine 2%, IA) premedication 15 minutes before MTX-071 IA administration single dose

Arm title	MTX-071 Group 3 - lido

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (5 ml lidocaine 2%, IA) premedication 15 minutes before MTX-071 IA administration single dose

Arm title	MTX-071 Group 4 - ropi
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (5 ml lidocaine 2%) premedication 15 minutes before MTX-071 IA administration single dose

Arm title	MTX-071 Group 5 - no LA
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

No local anaesthetics before MTX-071 IA administration single dose

Arm title	MTX-071 Group 6 - ropi cons
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (2 ml ropivacaine 1%, IA) within 1 minute before MTX-071 IA administration single dose

Arm title	MTX-071 Group 7 - ropi cons
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (2 ml ropivacaine 1%, IA) within 1 minute before MTX-071 IA administration single dose

Arm title	MTX-071 Group 8 - ropi cons
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Local anaesthetics (2 ml ropivacaine 1%, IA) within 1 minute before MTX-071 IA administration single dose

Number of subjects in period 1	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido
Started	3	3	3
Completed	3	3	3

Number of subjects in period 1	MTX-071 Group 4 - ropi	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons
Started	3	3	3
Completed	3	3	3

Number of subjects in period 1	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons
Started	3	3
Completed	3	3

Baseline characteristics

Reporting groups	
Reporting group title	MTX-071 Group 1 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 2 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 3 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 4 - ropi
Reporting group description: -	
Reporting group title	MTX-071 Group 5 - no LA
Reporting group description: -	
Reporting group title	MTX-071 Group 6 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 7 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 8 - ropi cons
Reporting group description: -	

Reporting group values	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (45-75 years)	3	3	3
Age continuous Units: years			
median	52.0	53.0	57.0
full range (min-max)	45 to 75	49 to 63	45 to 69
Gender categorical Units: Subjects			
Female	3	1	1
Male	0	2	2

Reporting group values	MTX-071 Group 4 - ropi	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons
Number of subjects	3	3	3
Age categorical Units: Subjects			
Adults (45-75 years)	3	3	3
Age continuous Units: years			
median	63.0	60.0	52.0
full range (min-max)	45 to 67	59 to 62	48 to 59
Gender categorical Units: Subjects			
Female	1	2	1
Male	2	1	2

Reporting group values	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons	Total
Number of subjects	3	3	24
Age categorical Units: Subjects			
Adults (45-75 years)	3	3	24
Age continuous Units: years			
median	53.0	59.0	
full range (min-max)	53 to 65	47 to 59	-
Gender categorical Units: Subjects			
Female	2	2	13
Male	1	1	11

End points

End points reporting groups

Reporting group title	MTX-071 Group 1 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 2 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 3 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 4 - ropi
Reporting group description: -	
Reporting group title	MTX-071 Group 5 - no LA
Reporting group description: -	
Reporting group title	MTX-071 Group 6 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 7 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 8 - ropi cons
Reporting group description: -	

Primary: Treatment-emergent adverse events

End point title	Treatment-emergent adverse events[1]

End point description:

End point type	Primary

End point timeframe:

From first study drug administration up to last observation i.e. 6 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive

End point values	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido	MTX-071 Group 4 - ropi
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Subjects				
At least one TEAE	3	2	3	3
At least one serious TEAE	0	0	0	0
At least one TEAE leading to death	0	0	0	0
At least one grade 1 TEAE as worst severity	1	1	1	2
At least one grade 2 TEAE as worst severity	1	0	2	1
At least one grade 3 TEAE as worst severity	1	1	0	0
At least one grade 4 TEAE as worst severity	0	0	0	0
At least one TEAE drug discontinued temporarily	0	0	0	0

At least one TEAE drug discontinued permanently	0	0	0	0
At least one treatment-related TEAE	3	2	2	2

End point values	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Subjects				
At least one TEAE	3	2	3	3
At least one serious TEAE	0	0	0	0
At least one TEAE leading to death	0	0	0	0
At least one grade 1 TEAE as worst severity	1	1	1	1
At least one grade 2 TEAE as worst severity	2	1	2	2
At least one grade 3 TEAE as worst severity	0	0	0	0
At least one grade 4 TEAE as worst severity	0	0	0	0
At least one TEAE drug discontinued temporarily	0	0	0	0
At least one TEAE drug discontinued permanently	0	0	0	0
At least one treatment-related TEAE	2	1	3	3

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline - treated knee in motion last 2 days

End point title	VAS efficacy changes from baseline - treated knee in motion last 2 days

End point description:

The severity of arthritis pain in subject's knee was assessed using a 100-millimeter (mm) VAS ranging from 0 mm = no pain and 100 mm = most severe pain. Higher score indicated more pain

End point type	Secondary

End point timeframe:

Baseline, 7 days, 30 days, 90 days and 180 days after injection

End point values	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido	MTX-071 Group 4 - ropi
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				

Day 7	-56.67 (± 35.921)	-30.67 (± 39.107)	-34.00 (± 36.715)	-37.50 (± 47.389)
Day 30	-63.00 (± 17.692)	-33.00 (± 39.585)	-40.33 (± 28.589)	-42.00 (± 49.568)
Day 90	-62.00 (± 28.583)	-21.33 (± 31.214)	-46.33 (± 16.503)	-53.33 (± 15.177)
Day 180	-63.33 (± 25.325)	-35.33 (± 14.742)	-33.67 (± 27.025)	-40.00 (± 28.000)

End point values	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-8.00 (± 24.269)	-45.67 (± 34.078)	-26.33 (± 23.288)	-31.33 (± 16.921)
Day 30	-25.33 (± 11.590)	-45.00 (± 35.553)	-30.67 (± 18.930)	-41.67 (± 13.051)
Day 90	-34.33 (± 15.885)	-41.33 (± 37.448)	-46.00 (± 4.243)	-51.00 (± 4.000)
Day 180	-37.00 (± 13.856)	-49.33 (± 10.786)	-50.33 (± 23.159)	-35.33 (± 20.207)

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline - treated knee in rest last 2 days

End point title	VAS efficacy changes from baseline - treated knee in rest last 2 days

End point description:

The severity of arthritis pain in subject's knee was assessed using a 100-millimeter (mm) VAS ranging from 0 mm = no pain and 100 mm = most severe pain. Higher score indicated more pain

End point type	Secondary

End point timeframe:

Baseline, 7 days, 30 days, 90 days and 180 days after injection.

End point values	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido	MTX-071 Group 4 - ropi
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-48.33 (± 27.429)	-29.67 (± 9.074)	-18.00 (± 25.159)	-34.67 (± 41.041)

Day 30	-54.33 (± 18.717)	-22.33 (± 18.556)	-32.33 (± 10.263)	-32.00 (± 36.428)
Day 90	-55.67 (± 26.558)	-12.33 (± 15.373)	-30.00 (± 14.731)	-35.67 (± 40.129)
Day 180	-55.67 (± 26.633)	-27.67 (± 11.060)	-16.33 (± 31.182)	-25.67 (± 23.692)

End point values	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-8.33 (± 16.010)	-17.00 (± 26.963)	-18.33 (± 18.009)	-1.67 (± 7.767)
Day 30	-12.67 (± 6.807)	-15.67 (± 28.219)	-14.33 (± 20.207)	-9.00 (± 14.107)
Day 90	-13.33 (± 8.145)	-11.33 (± 43.004)	-35.00 (± 1.414)	-17.00 (± 7.211)
Day 180	-18.33 (± 14.468)	-21.00 (± 22.068)	-33.33 (± 26.312)	-0.33 (± 22.811)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in total WOMAC score versus baseline

End point title	Changes in total WOMAC score versus baseline

End point description:

WOMAC: Self-administered, disease-specific questionnaire, which assesses clinically important, subject-relevant symptoms for pain, stiffness and physical function in subjects with osteoarthritis (OA of the hip and/or knee). The WOMAC composite index was the sum of 24 individual questions regarding subscales of pain, stiffness and physical function (for each item score range: 0 [minimum] to 4 [maximum], higher score indicating worse study joint condition). Total score was sum of the 3 subscale scores, giving a possible overall score range of 0 (minimum) to 96 (maximum). Higher score indicating the worse level of pain, stiffness and physical function.

End point type	Secondary

End point timeframe:

Baseline, 7 days, 30 days, 90 days and 180 days after injection.

End point values	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido	MTX-071 Group 4 - ropi
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-34.7 (± 17.93)	-18.7 (± 11.24)	-24.0 (± 26.89)	-28.6 (± 10.71)
Day 30	-47.3 (± 8.62)	-22.0 (± 15.87)	-30.7 (± 15.95)	-29.3 (± 9.45)
Day 90	-47.7 (± 23.86)	-14.7 (± 9.71)	-26.7 (± 17.47)	-26.1 (± 5.68)
Day 180	-44.3 (± 23.46)	-24.3 (± 11.72)	-20.0 (± 7.21)	-13.0 (± 21.66)

End point values	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-15.0 (± 10.39)	-24.7 (± 30.24)	-12.0 (± 17.44)	-18.5 (± 3.54)
Day 30	-21.0 (± 18.08)	1.0 (± 25.46)	-9.3 (± 19.09)	-35.00 (± 20.52)
Day 90	-25.0 (± 18.38)	-14.0 (± 14.73)	-18.7 (± 11.24)	-39.3 (± 15.50)
Day 180	-17.0 (± 7.00)	-3.3 (± 26.54)	-16.3 (± 9.45)	-27.0 (± 14.53)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first study drug administration up to last observation i.e. 6 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	MTX-071 Group 1 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 2 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 3 - lido
Reporting group description: -	
Reporting group title	MTX-071 Group 4 - ropi
Reporting group description: -	
Reporting group title	MTX-071 Group 5 - no LA
Reporting group description: -	
Reporting group title	MTX-071 Group 6 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 7 - ropi cons
Reporting group description: -	
Reporting group title	MTX-071 Group 8 - ropi cons
Reporting group description: -	

Serious adverse events	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MTX-071 Group 4 - ropi	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons	

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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: 0 %

Non-serious adverse events	MTX-071 Group 1 - lido	MTX-071 Group 2 - lido	MTX-071 Group 3 - lido
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	3 / 3 (100.00%)
Injury, poisoning and procedural complications			
Wasp sting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Low blood pressure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Follicular hyperplasia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Feeling of warmth			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flu-like symptoms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sweating			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cervicobrachalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Knee pain			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Knee pressure			

subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Leg pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rib contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stiffness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bladder infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flu			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	MTX-071 Group 4 - ropi	MTX-071 Group 5 - no LA	MTX-071 Group 6 - ropi cons
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	2 / 3 (66.67%)
Injury, poisoning and procedural complications			

Wasp sting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Low blood pressure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Follicular hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Feeling of warmth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flu-like symptoms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sweating			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cervicobrachalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Knee pain			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Knee pressure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leg pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rib contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stiffness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Bladder infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flu			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	MTX-071 Group 7 - ropi cons	MTX-071 Group 8 - ropi cons	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	
Injury, poisoning and procedural complications			
Wasp sting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Low blood pressure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Follicular hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Feeling of warmth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Flu-like symptoms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Sweating			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

Cervicobrachalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Joint stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Knee pain			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	
occurrences (all)	1	1	
Knee pressure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Leg pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Rib contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bladder infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Flu			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2018	- Addition up to two extra cohorts of 3 patients and extend the sample size from 18 to 24 patients maximum - Investigate the intra-articular administration of 2ml 1% ropivacaine immediately before MTX-071 administration (less than 1 min. interval, consecutive administration) through the same needle left in place for both administrations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported