Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Single Dose Phase IIb Exploratory Study to Document the Clinical Effects and Safety of Intra-articular Injections of Lopain (MTX-071) in Patients With Chronic Osteoarthritic Knee Joint Pain (Part 1 and Part 3) With Exploratory Pharmacokinetics (Part 3) and of Higher Doses or Consecutive Administrations With Local Anesthetics With Exploratory Pharmacokinetics (Part 2)

Summary

EudraCT number	2018-000818-37
Trial protocol	AT SK HR
Global end of trial date	26 January 2023

Results information

Result version number	v2 (current)
This version publication date	06 July 2024
First version publication date	11 February 2024
Version creation reason	• New data added to full data set Adverse event data need to be updated.

Trial information

Trial identification

Sponsor protocol code	MTX-071-P03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Grünenthal GmbH
Sponsor organisation address	Zieglerstr. 6, Aachen, Germany, 52099
Public contact	Grünenthal Trial Information Desk, Grünenthal GmbH, +49 241 569 3223, Clinical-trials@grunenthal.com
Scientific contact	Grünenthal Trial Information Desk, Grünenthal GmbH, +49 241 569 3223, 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	31 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1, 2: To compare the pain reduction effects (absolute and relative) at 3 months and 6 months of intra articular (IA) injections of different dose levels of MTX-071 (Lopain) relative to placebo in subjects with chronic osteoarthritic knee joint pain
Part 3: To compare the pain reduction effects (absolute and relative) at 3 months and 6 months of IA injections of different dose levels of MTX-071 (Lopain) relative to placebo in a narrowed subjects population having insufficient pain relief and being unsatisfied with optimized Standard of Care (including corticosteroids, hyaluronic acid, NSAIDs, opioids, non-pharmacological treatment).

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice guidelines, the ethical principles that have their origins in the Declaration of Helsinki, and the applicable local laws and regulations. The regulatory authority approved the trial as required by national regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2018
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	Slovakia: 54
Country: Number of subjects enrolled	Croatia: 14
Country: Number of subjects enrolled	Austria: 93
Worldwide total number of subjects	161
EEA total number of subjects	161

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)	96
From 65 to 84 years	65
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 7 sites in 3 countries between 23 October 2018 and 26 Jan 2023.

Pre-assignment

Screening details:

The study was conducted in 3 parts: Part 1, Part 2 and Part 3. A total of 161 subjects were enrolled and treated in the study.

Period 1

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

Arms

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

Arm description:

Subjects received a single 5 millilitres (mL) IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 1 - MTX-071 Group 2

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 more minute of pre-treatment with ropivacaine on Day 0 in Part 1.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 1 - Placebo

Arm description:

Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received IA injection of placebo matched to MTX-071 to the knee.

Arm title	Part 2 - MTX-071 Group 1

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 2 - MTX-071 Group 2

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 2 - MTX-071 Group 3

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 2 - MTX-071 Group 4

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.

Arm type	Experimental

Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 2 - Placebo

Arm description:

Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received IA injection of placebo matched to MTX-071 to the knee.

Arm title	Part 3 - MTX-071 Group 1

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 3 - MTX-071 Group 2

Arm description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.

Arm type	Experimental
Investigational medicinal product name	MTX-071
Investigational medicinal product code	RTX-GRT7039
Other name	Lopain
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received 5 mL MTX-071 IA injection to the knee.

Arm title	Part 3 - Placebo

Arm description:

Subjects received single IA injection of placebo matched to MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

Subjects received IA injection of placebo matched to MTX-071 to the knee.

Number of subjects in period 1	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo
Started	24	23	20
Completed	22	20	18
Not completed	2	3	2
Consent withdrawn by subject	1	2	-
Adverse event	-	-	-
Serious adverse event	-	-	1
Lost to follow-up	1	1	-
Therapeutic procedure	-	-	-
Lack of efficacy	-	-	1
Protocol deviation	-	-	-

Number of subjects in period 1	Part 2 - MTX-071 Group 1	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3
Started	11	5	10
Completed	9	5	9
Not completed	2	0	1
Consent withdrawn by subject	-	-	-
Adverse event	1	-	-
Serious adverse event	1	-	-
Lost to follow-up	-	-	1
Therapeutic procedure	-	-	-
Lack of efficacy	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Part 2 - MTX-071 Group 4	Part 2 - Placebo	Part 3 - MTX-071 Group 1
Started	7	7	18
Completed	5	6	16
Not completed	2	1	2
Consent withdrawn by subject	-	1	-
Adverse event	-	-	2
Serious adverse event	-	-	-
Lost to follow-up	-	-	-

Therapeutic procedure	1	-	-
Lack of efficacy	-	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo
Started	18	18
Completed	17	17
Not completed	1	1
Consent withdrawn by subject	1	-
Adverse event	-	1
Serious adverse event	-	-
Lost to follow-up	-	-
Therapeutic procedure	-	-
Lack of efficacy	-	-
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 millilitres (mL) IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 1 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 more minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 1 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 2 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.	
Reporting group title	Part 2 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 2 - MTX-071 Group 3
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.	
Reporting group title	Part 2 - MTX-071 Group 4
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 2 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 3 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	
Reporting group title	Part 3 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	
Reporting group title	Part 3 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	

Reporting group values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo
Number of subjects	24	23	20

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	60.7	62.5	62.2
standard deviation	± 7.88	± 6.95	± 9.22
Gender categorical Units: Subjects			
Female	17	14	16
Male	7	9	4

Reporting group values	Part 2 - MTX-071 Group 1	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3
Number of subjects	11	5	10
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	66.3	64.2	66.2
standard deviation	± 9.48	± 9.44	± 9.47
Gender categorical Units: Subjects			
Female	7	5	7
Male	4	0	3

Reporting group values	Part 2 - MTX-071 Group 4	Part 2 - Placebo	Part 3 - MTX-071 Group 1
Number of subjects	7	7	18
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	61.0	68.9	63.2
standard deviation	± 5.03	± 7.17	± 8.50
Gender categorical Units: Subjects			
Female	3	3	13
Male	4	4	5

Reporting group values	Part 3 - MTX-071 Group 2	Part 3 - Placebo	Total
Number of subjects	18	18	161
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	61.0	64.1	
standard deviation	± 7.96	± 7.46	-

Gender categorical Units: Subjects			
Female	11	13	109
Male	7	5	52

End points

End points reporting groups

Reporting group title	Part 1 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 millilitres (mL) IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 1 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 more minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 1 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.	
Reporting group title	Part 2 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.	
Reporting group title	Part 2 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 2 - MTX-071 Group 3
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.	
Reporting group title	Part 2 - MTX-071 Group 4
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 2 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.	
Reporting group title	Part 3 - MTX-071 Group 1
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	
Reporting group title	Part 3 - MTX-071 Group 2
Reporting group description:	
Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	
Reporting group title	Part 3 - Placebo
Reporting group description:	
Subjects received single IA injection of placebo matched to MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.	

Primary: Absolute Reduction From Baseline in the Visual Analog Scale (VAS) Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6

End point title	Absolute Reduction From Baseline in the Visual Analog Scale (VAS) Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6[1]

End point description:

Subjects were asked to document the severity of pain on motion and for pain on rest on individual VAS. The subject was asked to mark a position on two 100 millimetre (mm) (where 0 = no pain and 100 = maximum pain) horizontal lines that correspond to the intensity of the pain of the treated knee as an average of the last two days, respectively at rest and on motion. The absolute reduction of the VAS for pain on motion as average of the last two days will be evaluated as the absolute change, defined as: VAS score at post-baseline visit - VAS score at baseline visit. Analysis was performed on intent to treat (ITT) population which included all randomized subject who received study drug and had at least one efficacy assessment at Baseline and post-baseline. Here, 'n' = subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Baseline, Months 3 and 6

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	19	11
Units: millimetre				
arithmetic mean (standard deviation)				
Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-37.43 (± 19.797)	-36.68 (± 34.167)	-17.00 (± 23.098)	-39.75 (± 39.764)
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-33.52 (± 22.894)	-41.48 (± 32.576)	-28.26 (± 25.029)	-46.49 (± 29.164)

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	7
Units: millimetre				
arithmetic mean (standard deviation)				
Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-40.20 (± 35.316)	-30.25 (± 25.640)	-34.14 (± 31.757)	-8.50 (± 19.994)
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-43.40 (± 34.883)	-22.00 (± 26.491)	-38.60 (± 29.905)	-3.42 (± 19.371)

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: millimetre				
arithmetic mean (standard deviation)				

Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-22.33 (± 30.662)	-33.39 (± 23.655)	-31.11 (± 30.932)	
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-19.78 (± 30.001)	-24.09 (± 27.583)	-34.21 (± 29.226)	

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change From Baseline in the Visual Analog Scale (VAS) Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6

End point title	Percent Change From Baseline in the Visual Analog Scale (VAS) Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6[2]

End point description:

Subjects were asked to document the severity of pain on motion and for pain on rest on individual VAS. The subject was asked to mark a position on two 100 mm (where 0 = no pain and 100 = maximum pain) horizontal lines that correspond to the intensity of the pain of the treated knee as an average of the last two days, respectively at rest and on motion. The percentage change of the VAS for pain on motion as average of the last two days will be evaluated as the relative change, defined as: 100% x ([VAS score at post-baseline visit] - [VAS score at baseline visit])/ (VAS score at baseline visit). Analysis was performed on ITT population. Here, 'n' =subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Baseline, Month 3 and 6

Notes:

[2] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	19	11
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-56.57 (± 27.982)	-49.71 (± 47.529)	-28.97 (± 36.941)	-49.45 (± 53.671)
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-51.25 (± 37.599)	-58.61 (± 47.182)	-50.29 (± 42.821)	-64.65 (± 37.866)

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	7
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-54.56 (± 47.355)	-56.13 (± 42.347)	-51.04 (± 46.856)	-19.18 (± 42.058)
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-58.26 (± 43.402)	-39.23 (± 43.903)	-57.76 (± 43.448)	-8.30 (± 40.908)

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	-31.16 (± 42.824)	-45.98 (± 31.448)	-46.94 (± 51.966)	
Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	-27.96 (± 42.305)	-33.32 (± 43.098)	-54.28 (± 44.301)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Greater Than or Equal to (>=) 50% and >= 70% Decrease From Baseline in VAS Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6

End point title	Percentage of Subjects With Greater Than or Equal to (>=) 50% and >= 70% Decrease From Baseline in VAS Scores for Pain on Motion in the Target Knee Joint at Months 3 and 6

End point description:

Subjects were asked to document the severity of pain on motion and for pain on rest on individual VAS. The subject was asked to mark a position on two 100 mm (where 0 = no pain and 100 = maximum pain) horizontal lines that correspond to the intensity of the pain of the treated knee as an average of the last two days, respectively at rest and on motion. Percentage of subjects with >= 50% and >= 70% reduction from Baseline in VAS scores for pain on motion at Months 3 and 6 are reported in this endpoint. Analysis was performed on ITT population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Months 3 and 6

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	19	11
Units: percentage of subjects				
number (not applicable)				
>= 50%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	60.9	52.6	33.3	60.0
>=50%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	63.6	65.0	52.9	75.0
>= 70%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	43.5	47.4	16.7	40.0
>=70%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	31.8	55.0	47.1	50.0

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	7
Units: percentage of subjects				
number (not applicable)				
>= 50%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	60.0	60.0	57.1	40.0
>=50%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	60.0	50.0	60.0	16.7
>= 70%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	60.0	40.0	57.1	0
>=70%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	40.0	30.0	60.0	16.7

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: percentage of subjects				
number (not applicable)				
>= 50%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	55.6	38.9	55.6	
>=50%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	31.3	41.2	52.9	
>= 70%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18)	16.7	16.7	38.9	
>=70%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17)	18.8	23.5	47.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Total Scores at Months 3 and 6: Part 1 and 2

End point title	Percent Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Total Scores at Months 3 and 6: Part 1 and 2[3]

End point description:

WOMAC is used to assess pain, stiffness, and physical function in subjects with hip and/or knee osteoarthritis (OA). It consists of 24 items divided into 3 subscales: Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing; Stiffness (2 items): after first waking and later in the day; Physical Function (17 items): stair use, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in/out of bath, sitting, getting on / off toilet, heavy household duties, light household duties. Each item was scored on a 5-point Likert scale ranging 0 to 4 and the scores are summed for items in each subscale, with possible ranges as follows: pain score=0-20, stiffness score=0-8, physical function score=0-68.

Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations. ITT population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Month 3 and 6

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for all applicable arms.

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	19	11
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=22,19,18,10,5,10,7,6)	-36.55 (± 30.189)	-35.59 (± 45.713)	-18.22 (± 48.508)	-46.44 (± 37.723)
Month 6 (n=22,19,17,8,5,10,5,6)	-40.84 (± 24.783)	-42.44 (± 56.651)	-28.63 (± 63.077)	-44.88 (± 39.702)

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	7
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=22,19,18,10,5,10,7,6)	-27.04 (± 34.262)	-26.27 (± 64.208)	-38.09 (± 32.723)	-20.82 (± 27.887)
Month 6 (n=22,19,17,8,5,10,5,6)	-29.30 (± 41.600)	-21.22 (± 53.451)	-42.48 (± 23.602)	18.15 (± 55.757)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Total Scores at Months 3 and 6: Part 3

End point title	Percent Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Total Scores at Months 3 and 6: Part 3[4]

End point description:

WOMAC is used to assess pain, stiffness, and physical function in subjects with hip and/or knee OA. It consists of 24 items divided into 3 subscales: Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing; Stiffness (2 items): after first waking and later in the day; Physical Function (17 items): stair use, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in/out of bath, sitting, getting on / off toilet, heavy household duties, light household duties. Each item was scored on a 11-point numeric rating scale ranging 0 to 10 and the scores are summed for items in each subscale, with possible ranges as follows: pain score = 0-50, stiffness score = 0-20, physical function score = 0-170. Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations. ITT population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Months 3 and 6

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for all applicable arms.

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: percent change				
arithmetic mean (standard deviation)				
Month 3 (n=18,18,18)	-21.91 (± 33.203)	-35.58 (± 39.477)	-36.86 (± 49.661)	
Month 6 (n=16,17,17)	-22.74 (± 35.132)	-16.47 (± 84.916)	-42.24 (± 38.514)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Improvement in Patient Global Impression of Change (PGIC) Score at Day 8, Month 1, 3 and 6

End point title	Percentage of Subjects With Improvement in Patient Global Impression of Change (PGIC) Score at Day 8, Month 1, 3 and 6[5]

End point description:

The questionnaire reflects a subject's belief about the efficacy of treatment. The PGIC is a 7-point scale (1-7) depicting a subject's rating of overall improvement. Subjects rate their change as 1 = "very much improved," 2 = "much improved," 3 = "minimally improved," 4 = "no change," 5 = "minimally worse," 6 = "much worse," or 7 = "very much worse." Lower values represent a better outcome. Analysis was performed on ITT population. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was planned to be collected and reported for Part 3 only.

End point type	Secondary

End point timeframe:

Day 8, Month 1, 3 and 6

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for all applicable arms.

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: percentage of subjects				
number (not applicable)				
Day 8	66.67	83.33	77.78	
Month 1	61.11	83.33	72.22	
Month 3	66.67	50.00	72.22	
Month 6	56.25	64.71	82.35	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Specific Functional Scale (PSFS) Total Score at Months 3 and 6

End point title	Change From Baseline in Patient Specific Functional Scale (PSFS) Total Score at Months 3 and 6[6]

End point description:

PSFS is a three-item instrument, administered verbally, that is used to evaluate whether a health condition impacts a subject's ability to perform activities that are important to him/her. On the initial assessment, the subject is asked to identify "up to three important activities that you are unable to do or are having difficulty with as a result of your OA." Subject then provides a rating for each item, on an 11-point ordinal scale ranging from 0 ("unable to perform activity") to 10 ("able to perform activity at the same level as before the injury or problem"). During reassessments, the subject is prompted to re-rate the same three activities. The average of up to 3 specific activity scores was recorded, and the range of possible scores is 0 - 10. Total score = sum of activity scores/number of activities. Higher scores indicate less impairment. Analysis was performed on ITT population. Data for this endpoint was planned to be collected and reported for Part 3 only. Here, n = subjec

End point type	Secondary

End point timeframe:

Baseline, Months 3 and 6

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for all applicable arms.

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: score on a scale				
arithmetic mean (standard deviation)				
Month 3 (n = 18, 18, 18)	1.11 (± 1.674)	1.91 (± 1.427)	1.23 (± 1.890)	
Month 6 (n = 16, 17, 17)	1.18 (± 1.603)	1.60 (± 1.645)	1.86 (± 2.378)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An Adverse Event (AE) was any untoward medical occurrence in a subject administered a

pharmaceutical product and which did not necessarily had to have causal relationship with treatment. TEAEs were defined as AEs that occurred or worsened in severity between the first dose of the IMP until the end of follow up. A SAE was any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. Analysis was performed on all treated population.

End point type	Secondary

End point timeframe:

From Baseline up to Month 6

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	20	11
Units: subjects				
Any TEAEs	15	18	15	10
Any TESAEs	2	3	1	2

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	7
Units: subjects				
Any TEAEs	3	8	6	6
Any TESAEs	0	0	0	0

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: subjects				
Any TEAEs	16	17	14	
Any TESAEs	1	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximal VAS Scores During Day 1

End point title	Maximal VAS Scores During Day 1

End point description:

A 100 mm VAS was used to assess the subject's current pain. The subject rated their current pain from 0 (no pain) to 100 (worst possible pain). A negative value indicates improvement in symptoms. Analysis was performed on ITT population. Here, 'subjects analyzed' = subjects with available data for this

endpoint.

End point type	Secondary

End point timeframe:

0 hour, 0.5 hour, 1.5 hour and 3 hour post-dose on Day 1

End point values	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo	Part 2 - MTX-071 Group 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	23	19	11
Units: score on a scale				
arithmetic mean (standard deviation)	61.29 (± 24.451)	71.41 (± 24.644)	28.86 (± 19.866)	73.45 (± 24.407)

End point values	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3	Part 2 - MTX-071 Group 4	Part 2 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	10	7	4
Units: score on a scale				
arithmetic mean (standard deviation)	81.80 (± 34.120)	69.70 (± 21.756)	77.86 (± 16.767)	43.07 (± 26.276)

End point values	Part 3 - MTX-071 Group 1	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: score on a scale				
arithmetic mean (standard deviation)	22.28 (± 29.416)	74.58 (± 19.177)	36.47 (± 23.845)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to Month 6

Adverse event reporting additional description:

Analysis was performed on all treated population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Part 1 - MTX-071 Group 1

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 1.

Reporting group title	Part 1 - MTX-071 Group 2

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 more minute of pre-treatment with ropivacaine on Day 0 in Part 1.

Reporting group title	Part 1 - Placebo

Reporting group description:

Subjects received single IA injection of placebo matched to MTX-071 on Day 0 in Part 1.

Reporting group title	Part 2 - MTX-071 Group 1

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.

Reporting group title	Part 2 - MTX-071 Group 2

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.

Reporting group title	Part 2 - MTX-071 Group 3

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 2. "Consecutive" treatment required IA injection of investigational medicinal product within 1 minute after IA injection of ropivacaine.

Reporting group title	Part 2 - MTX-071 Group 4

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 15 minute of pre-treatment with ropivacaine on Day 0 in Part 2.

Reporting group title	Part 2 - Placebo

Reporting group description:

Subjects received single IA injection of placebo matched to MTX-071 on Day 0 in Part 2.

Reporting group title	Part 3 - MTX-071 Group 1

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.

Reporting group title	Part 3 - MTX-071 Group 2

Reporting group description:

Subjects received a single 5 mL IA injection of MTX-071 within 1 minute of pre-treatment with ropivacaine on Day 0 in Part 3.

Reporting group title	Part 3 - Placebo

Reporting group description:
Subjects received single IA injection of placebo matched to MTX-071 on Day 0 in Part 3.

Serious adverse events	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	3 / 23 (13.04%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (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
Nervous system disorders			
Lumbar radiculopathy			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (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
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 - MTX-071 Group 1	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)	0 / 5 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lumbar radiculopathy			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 - MTX-071 Group 4	Part 2 - Placebo	Part 3 - MTX-071 Group 1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lumbar radiculopathy			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	3 / 18 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary arterial stent insertion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Lumbar radiculopathy			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1 - MTX-071 Group 1	Part 1 - MTX-071 Group 2	Part 1 - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 24 (62.50%)	17 / 23 (73.91%)	15 / 20 (75.00%)
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood pressure fluctuation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Circulatory collapse			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Thrombophlebitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Dental care			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tooth extraction			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paronychia drainage			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cataract operation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	4
Feeling hot			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Application site joint warmth			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injection site joint swelling			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Chest pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Menopausal symptoms			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 20 (10.00%)
occurrences (all)	0	1	3
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Allergic sinusitis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pharyngeal paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Stress			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood glucose increased			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment depression			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Heart rate irregular			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Temperature difference of extremities			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Foreign body in eye			

subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Multiple injuries			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Postoperative wound complication			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Arrhythmia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 24 (8.33%)	3 / 23 (13.04%)	4 / 20 (20.00%)
occurrences (all)	3	7	7
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Burning feet syndrome			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral nerve paresis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Bone marrow oedema			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Diabetic retinopathy			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Maculopathy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Toothache			
subjects affected / exposed	0 / 24 (0.00%)	2 / 23 (8.70%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Liver disorder			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Scar pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal disorder			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 24 (12.50%)	3 / 23 (13.04%)	5 / 20 (25.00%)
occurrences (all)	3	7	5

Osteoarthritis			
subjects affected / exposed	2 / 24 (8.33%)	1 / 23 (4.35%)	2 / 20 (10.00%)
occurrences (all)	2	1	5
Pain in extremity			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Myalgia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Joint swelling			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Trigger finger			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Periarthritis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	7 / 24 (29.17%)	6 / 23 (26.09%)	7 / 20 (35.00%)
occurrences (all)	12	6	10
Arthritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	2	0

Joint warmth			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Osteoporosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pain in jaw			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Plantar fasciitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Synovial cyst			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 24 (4.17%)	2 / 23 (8.70%)	3 / 20 (15.00%)
occurrences (all)	1	2	4
Bronchitis			
subjects affected / exposed	0 / 24 (0.00%)	3 / 23 (13.04%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Influenza			

subjects affected / exposed	2 / 24 (8.33%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Laryngitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
COVID-19			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Coronavirus infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Tracheitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Borrelia infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Diverticulitis			

subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Post-acute COVID-1 9 syndrome			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 23 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2 - MTX-071 Group 1	Part 2 - MTX-071 Group 2	Part 2 - MTX-071 Group 3
Total subjects affected by non-serious adverse events			

subjects affected / exposed	10 / 11 (90.91%)	3 / 5 (60.00%)	8 / 10 (80.00%)
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood pressure fluctuation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Circulatory collapse			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dental care			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tooth extraction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paronychia drainage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cataract operation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Feeling hot			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Application site joint warmth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site joint swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chest pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menopausal symptoms			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Allergic sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngeal paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Temperature difference of extremities			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Foreign body in eye			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Multiple injuries			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Postoperative wound complication			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Extrasystoles			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Burning feet syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral nerve paresis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Bone marrow oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diabetic retinopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Maculopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Liver disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 5 (40.00%)	1 / 10 (10.00%)
occurrences (all)	1	4	1
Osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Joint effusion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Trigger finger			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Periarthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	6 / 11 (54.55%)	1 / 5 (20.00%)	5 / 10 (50.00%)
occurrences (all)	10	1	9
Arthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint warmth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Borrelia infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Post-acute COVID-1 9 syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 11 (9.09%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Part 2 - MTX-071 Group 4	Part 2 - Placebo	Part 3 - MTX-071 Group 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	6 / 7 (85.71%)	16 / 18 (88.89%)
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood pressure fluctuation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Circulatory collapse			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dental care			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tooth extraction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Paronychia drainage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cataract operation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Feeling hot			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Injection site pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Application site joint warmth			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injection site joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Menopausal symptoms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Allergic sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pharyngeal paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	4	0

Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Stress			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Temperature difference of extremities			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Foreign body in eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Multiple injuries			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Contusion			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Postoperative wound complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 7 (14.29%)	4 / 7 (57.14%)	5 / 18 (27.78%)
occurrences (all)	1	10	13
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Migraine			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Burning feet syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Peripheral nerve paresis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Bone marrow oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Diabetic retinopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Eye disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Maculopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Liver disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Erythema nodosum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Bladder irritation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3
Osteoarthritis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	4
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Trigger finger			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Periarthritis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 7 (28.57%)	10 / 18 (55.56%)
occurrences (all)	2	2	22
Arthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Joint warmth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Spinal pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Synovial cyst			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Coronavirus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Borrelia infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Post-acute COVID-1 9 syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Tooth infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 3 - MTX-071 Group 2	Part 3 - Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	13 / 18 (72.22%)	
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood pressure fluctuation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Circulatory collapse			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Thrombophlebitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			

Dental care			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Tooth extraction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Paronychia drainage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cataract operation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	3	2	
Feeling hot			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Application site joint warmth			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Inflammation			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Injection site joint swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injection site haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Menopausal symptoms			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Allergic sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Pharyngeal paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Restlessness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Stress			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	

Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood cholesterol increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Body temperature increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Electrocardiogram ST segment depression			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Heart rate irregular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Temperature difference of extremities			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	

Foreign body in eye			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Joint dislocation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Multiple injuries			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Wound			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Rib fracture			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Postoperative wound complication			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Extrasystoles			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Cardiac failure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 18 (22.22%)	2 / 18 (11.11%)	
occurrences (all)	9	9	
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Restless legs syndrome			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Burning feet syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Peripheral nerve paresis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Polyneuropathy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Head discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Bone marrow oedema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Diabetic retinopathy			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Eye disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Maculopathy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	3 / 18 (16.67%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Colitis ulcerative			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Liver disorder			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Dermatitis allergic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	4	0	
Erythema nodosum			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Scar pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Renal disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 18 (16.67%)	1 / 18 (5.56%)	
occurrences (all)	3	1	

Osteoarthritis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	3 / 18 (16.67%)	1 / 18 (5.56%)	
occurrences (all)	7	1	
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Joint effusion			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Joint swelling			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Trigger finger			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Periarthritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	5	
Rotator cuff syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	6 / 18 (33.33%)	4 / 18 (22.22%)	
occurrences (all)	8	9	
Arthritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	

Joint warmth			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Osteoporosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pain in jaw			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Plantar fasciitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Synovial cyst			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 18 (22.22%)	0 / 18 (0.00%)	
occurrences (all)	4	0	
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Influenza			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	5 / 18 (27.78%)	4 / 18 (22.22%)	
occurrences (all)	5	4	
Herpes zoster			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Coronavirus infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tracheitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Borrelia infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Diverticulitis			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Post-acute COVID-1 9 syndrome			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Tooth infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2018	Following changes were made: • The trial was extended to trial sites in Croatia; In some parts of the protocol, the IMP was called "MTX-071", which could have been interpreted as relating only to verum. To clarify, "MTX-071" was replaced by "MTX-071/placebo"; The time window for administration of IMP, which was already described in the information for the pharmacist, was added to the protocol; The determination of postmenopausal women was initially defined as "no menses for at least 24 months"; however, a follicle-stimulating hormone test was planned and mentioned in Section 8.3.10.7: laboratory assessments. The definition "postmenopausal as confirmed by follicle-stimulating hormone level" was added: contraceptive measures; Investigational medicinal product transport from the pharmacy to the trial sites was accepted in a ready-made syringe instead of the glass vial. This change was made upon advice from the participating pharmacists and investigators; A clarification was added to the randomisation numbers table indicating that it was just illustrating the principle and did not show the actual randomization numbers.
04 February 2019	Following changes were made: The trial was extended to trial sites in Austria and Croatia; A blinded interim analysis was planned with the first 3 subjects of each trial site (in total 9 subjects). As the number of trial sites had increased, the definition of the subjects to be analysed was changed to first 3 subjects of 3 trial sites; The time window for administration of premedication was aligned in different sections in the protocol.
12 July 2019	Following changes were done: The trial was extended to include administration of higher doses of RTX-GRT7039 (that had already been used in a Phase I trial) and a consecutive injection with a local anesthetic; The number of subjects to be included in Part 2 of the trial was added together with the planned treatment groups; An unblinded interim analysis (with no hold) of the efficacy (VAS) data of Part 1 was included to evaluate the evolution of the trial. The interim analysis was to take place after all subjects completed the 3-month VAS assessment; An option was added to perform the follow-up remotely.
19 December 2019	Following change was done: Voluntary blood sampling for pharmacokinetics at several timepoints on the day of injection was added for up to 7 subjects in Part 2.
13 April 2021	Following changes were done: The trial was extended with Part 3, to include an additional 60 subjects who were to receive RTX-GRT7039 or placebo consecutively with a local anesthetic; Two additional questionnaires (PGIC and PSFS) were added to investigate the effect of treatment on knee joint pain, compared to placebo; Subjects included in Part 3 of the trial were given the opportunity to receive a second injection with RTX-GRT7039 in case of recurring knee pain 6 months or 9 months after the first injection; The documentation of knee pain in the subject diary was changed to a weekly basis instead of a monthly basis; The documentation of knee pain at the trial site was updated to include the pain in the contra-lateral knee for at least 3 visits.
31 August 2021	Following changes were made: Voluntary blood sampling for pharmacokinetics at several timepoints on the day of injection was added for a minimum of 9 subjects in Part 3; The additional exploratory objectives and endpoints were updated to reflect the collection and analysis of blood samples for pharmacokinetics in Part 3.

30 March 2022	Following changes were made: The sponsor was changed from Mestex AG, Klosterberg 11, CH-4051 Basel, Switzerland to Grünenthal GmbH, 52099 Aachen, Germany; effective as of 01 Apr 2022. Associated changes to the author and key trial personnel were made; The IMP packaging and labeling information presented in the protocol were updated; The safety reporting procedure was adapted as Grünenthal Global Drug Safety prepared to takeover reporting to the competent authorities (safety reporting takeover took place on 28 Apr 2022) while the Safety Unit at QPS performed reporting to the ethics committee and investigators; The description of IMP handling in the protocol was updated with subsequent section renumbering.
18 August 2022	Following changes were made: The coordinating investigator was changed, and the respective details were updated: The medical monitor was changed, and the respective details were updated; The name and function on the sponsor signature page was changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported