

**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 | <ul style="list-style-type: none">• New data added to full data setAdverse 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 standard deviation | 60.7 ± 7.88 | 62.5 ± 6.95 | 62.2 ± 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 standard deviation | 66.3 ± 9.48 | 64.2 ± 9.44 | 66.2 ± 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 standard deviation | 61.0 ± 5.03 | 68.9 ± 7.17 | 63.2 ± 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 standard deviation | 61.0 ± 7.96 | 64.1 ± 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: $100\% \times ([\text{VAS score at post-baseline visit}] - [\text{VAS score at baseline visit}]) / (\text{VAS score at baseline visit})$. 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 (\geq) 50% and \geq 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 (\geq) 50% and \geq 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 \geq 50% and \geq 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) | | | | |
| \geq 50%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18) | 60.9 | 52.6 | 33.3 | 60.0 |
| \geq 50%: Month 6 (n=22,20,17,8,5,10,5,6,16,17,17) | 63.6 | 65.0 | 52.9 | 75.0 |
| \geq 70%: Month 3 (n=23,19,18,10,5,10,7,5,18,18,18) | 43.5 | 47.4 | 16.7 | 40.0 |
| \geq 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 = subject

| | |
|----------------|-----------|
| 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 (\pm 24.451) | 71.41 (\pm 24.644) | 28.86 (\pm 19.866) | 73.45 (\pm 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 (\pm 34.120) | 69.70 (\pm 21.756) | 77.86 (\pm 16.767) | 43.07 (\pm 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 (\pm 29.416) | 74.58 (\pm 19.177) | 36.47 (\pm 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 |
|-----------------------|------------------|

| 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 occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 20 (0.00%) 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 | | | |

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|-----------------------------|----------------|----------------|----------------|
| 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-19 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 |

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

| | | | |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 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 occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Peripheral nerve paresis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Polyneuropathy subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Head discomfort subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Blood and lymphatic system disorders Bone marrow oedema subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Eye disorders Cataract subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Diabetic retinopathy subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Eye disorder subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Maculopathy subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 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 occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Erythema nodosum subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Scar pain subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Renal and urinary disorders Bladder irritation subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Renal disorder subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Endocrine disorders Basedow's disease subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 2 / 5 (40.00%) 4 | 1 / 10 (10.00%) 1 |
| Osteoarthritis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 5 (20.00%) 1 | 2 / 10 (20.00%) 2 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 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-19 syndrome subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Rhinitis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 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 occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Blood pressure fluctuation subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Hypertension | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Circulatory collapse subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Thrombophlebitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Surgical and medical procedures | | | |
| Dental care subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Tooth extraction subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 18 (0.00%) 0 |
| Paronychia drainage subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Cataract operation subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | 0 / 18 (0.00%) 0 |
| Feeling hot subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 1 / 7 (14.29%) 1 | 0 / 18 (0.00%) 0 |
| Injection site pain subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 2 / 18 (11.11%) 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Diabetic retinopathy subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 2 |
| Eye disorder subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Maculopathy subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Renal disorder subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Endocrine disorders Basedow's disease subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 2 / 18 (11.11%) 3 |
| Osteoarthritis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | 2 / 18 (11.11%) 4 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Joint effusion subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Joint swelling subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 1 / 18 (5.56%) 2 |
| Trigger finger subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Intervertebral disc protrusion subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 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-19 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Gout subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 7 (0.00%) 0 | 0 / 18 (0.00%) 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 occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 0 | |
| Blood pressure fluctuation subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 0 | |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 0 | |
| Hypertension subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 18 (5.56%) 1 | |
| Circulatory collapse subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 0 | |
| Hypotension subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 0 | |
| Thrombophlebitis subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 18 (0.00%) 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 occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 18 (0.00%) 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-19 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. |

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| 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