



Clinical trial results:

An open label, dose-escalating phase I/IIa study to determine the safety and clinical effects of intra-articular injections of Lopain (MTX-071) in patients with chronic osteoarthritic knee joint pain after a single dose (Part 1) and after repeated dose administration (Part 2)

Summary

EudraCT number	2015-001981-24
Trial protocol	BE
Global end of trial date	24 April 2019

Results information

Result version number	v1 (current)
This version publication date	14 May 2021
First version publication date	14 May 2021

Trial information

Trial identification

Sponsor protocol code	MTX-071-P01
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Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 April 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part I:

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

Part II:

The primary objective was the safety and tolerability of a second and a third intra-articular injection of MTX-071 on the incidence, nature and severity of AES/SAEs potentially causally related with the study medication.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

20 subjects were enrolled.

Period 1

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

Arms

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

Arm description: -

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

Dosage and administration details:

Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a single dose of MTX-071

Arm title	MTX-071 Group 5 - PA (Part 1)
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Arm description: -

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

Dosage and administration details:

No local anesthetics, with oral premedication (600 mg ibuprofen) and a single dose of MTX-071

Arm title	MTX-071 Group 2 - (Part 1)
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Arm description: -

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

Dosage and administration details:

Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a single dose of MTX-071

Arm title	MTX-071 Group 6 - PA (Part 1)
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Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use
Dosage and administration details:	
No local anesthetics, with oral premedication (600 mg ibuprofen) and a single dose of MTX-071	
Arm title	MTX-071 Group 3 - (Part 1)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use
Dosage and administration details:	
Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a single dose of MTX-071	
Arm title	MTX-071 Group 7 - PA (Part 1)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use
Dosage and administration details:	
No local anesthetics, with oral premedication (600 mg ibuprofen) and a single dose of MTX-071	
Arm title	MTX-071 Group 4 - (Part 1)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Lopain
Investigational medicinal product code	MTX-071
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraarticular use
Dosage and administration details:	
Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a single dose of MTX-071	

Number of subjects in period 1	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)
Started	3	4	3
Completed	3	4	3
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	MTX-071 Group 6 - PA (Part 1)	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)
Started	3	3	1
Completed	3	3	0
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	MTX-071 Group 4 - (Part 1)
Started	3
Completed	3
Not completed	0
Consent withdrawn by subject	-

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	MTX-071 Group 1 - (Part 2) second injection

Arm description: -

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

Dosage and administration details:

Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a second single dose of MTX-071

Arm title	MTX-071 Group 5 - PA (Part 2) second injection
Arm description: -	
Arm type	Experimental

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

Dosage and administration details:

No local anesthetics, with oral premedication (600 mg ibuprofen) and a second single dose of MTX-071

Arm title	MTX-071 Group 1 - (Part 2) third injection
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Arm description: -

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

Dosage and administration details:

Local anesthetics (5 mL of ropivacaine 0.5%, IA), without oral premedication and a third single dose of MTX-071

Number of subjects in period 2	MTX-071 Group 1 - (Part 2) second injection	MTX-071 Group 5 - PA (Part 2) second injection	MTX-071 Group 1 - (Part 2) third injection
Started	7	1	3
Completed	2	1	3
Not completed	5	0	0
Consent withdrawn by subject	2	-	-
failure to continue	3	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall
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Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	20	20	
Age categorical			
Units: Subjects			
From 47 - 75 years	20	20	
Age continuous			
Units: years			
median	57.5		
full range (min-max)	47 to 75	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	10	10	

End points

End points reporting groups

Reporting group title	MTX-071 Group 1 - (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 5 - PA (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 2 - (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 6 - PA (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 3 - (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 7 - PA (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 4 - (Part 1)
Reporting group description: -	
Reporting group title	MTX-071 Group 1 - (Part 2) second injection
Reporting group description: -	
Reporting group title	MTX-071 Group 5 - PA (Part 2) second injection
Reporting group description: -	
Reporting group title	MTX-071 Group 1 - (Part 2) third injection
Reporting group description: -	
Subject analysis set title	MTX-071 Group 1 - second injection
Subject analysis set type	Intention-to-treat
Subject analysis set description: efficacy	
Subject analysis set title	MTX-071 Group 1 - third injection
Subject analysis set type	Intention-to-treat
Subject analysis set description: efficacy	

Primary: Treatment-emergent adverse events (Part 1)

End point title	Treatment-emergent adverse events (Part 1) ^[1]
End point description: Analysis was performed on Safety population i.e. subjects were analysed according to the treatment actually received.	
End point type	Primary
End point timeframe: Continuous assessment up to 6 months after injection.	

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: Descriptively only

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: subjects				
At least one TEAE	3	4	3	3
At least one serious TEAE	0	0	0	0
At least one TEAE leading to death	0	0	0	0
At least one grade 1 TEAE as worst severity	0	2	1	0
At least one grade 2 TEAE as worst severity	2	1	1	1
At least one grade 3 TEAE as worst severity	1	1	1	2
At least one grade 4 TEAE as worst severity	0	0	0	0
At least one TEAE drug discontinued temporarily	0	0	0	0
At least one TEAE drug discontinued permanently	0	0	0	0
At least one treatment-related TEAE	2	4	2	3

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: subjects				
At least one TEAE	3	1	3	
At least one serious TEAE	0	0	0	
At least one TEAE leading to death	0	0	0	
At least one grade 1 TEAE as worst severity	0	0	2	
At least one grade 2 TEAE as worst severity	1	0	0	
At least one grade 3 TEAE as worst severity	2	1	1	
At least one grade 4 TEAE as worst severity	0	0	0	
At least one TEAE drug discontinued temporarily	0	0	0	
At least one TEAE drug discontinued permanently	0	0	0	
At least one treatment-related TEAE	3	1	3	

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-emergent adverse events (Part 2)

End point title	Treatment-emergent adverse events (Part 2) ^[2]
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End point description:

Analysis was performed on Safety population i.e. subjects were analysed according to the treatment actually received.

End point type	Primary
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End point timeframe:

Continuous assessment up to 6 months after injection.

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: Descriptively only

End point values	MTX-071 Group 1 - (Part 2) second injection	MTX-071 Group 5 - PA (Part 2) second injection	MTX-071 Group 1 - (Part 2) third injection	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	3	
Units: subjects				
At least one TEAE	6	1	3	
At least one serious TEAE	0	0	0	
At least one TEAE leading to death	0	0	0	
At least one grade 1 TEAE as worst severity	2	0	0	
At least one grade 2 TEAE as worst severity	3	1	3	
At least one grade 3 TEAE as worst severity	1	0	0	
At least one grade 4 TEAE as worst severity	0	0	0	
At least one TEAE drug discontinued temporarily	0	0	0	
At least one TEAE drug discontinued permanently	0	0	0	
At least one treatment-related TEAE	4	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 1) - treated knee in motion over last 2 days

End point title	VAS efficacy changes from baseline (Part 1) - treated knee in motion over last 2 days
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End point description:

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

End point type	Secondary
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End point timeframe:

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

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-20.33 (± 32.808)	-36.50 (± 20.984)	-67.00 (± 17.776)	-56.00 (± 18.735)
Day 30	-40.67 (± 15.144)	-47.25 (± 11.266)	-65.00 (± 23.388)	-52.33 (± 20.502)
Day 90	-44.00 (± 8.718)	-39.50 (± 22.368)	-53.00 (± 8.888)	-41.33 (± 18.930)
Day 180	-42.67 (± 11.240)	-18.75 (± 17.933)	-66.33 (± 23.094)	-41.00 (± 28.054)

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	0 ^[3]	3	
Units: score				
arithmetic mean (standard deviation)				
Day 7	-23.67 (± 33.787)	()	-53.33 (± 21.362)	
Day 30	-33.00 (± 37.172)	()	-55.67 (± 17.388)	
Day 90	-32.67 (± 38.027)	()	-60.67 (± 6.110)	
Day 180	-38.67 (± 33.137)	()	-56.00 (± 6.083)	

Notes:

[3] - Subject withdraw consent

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 1) - treated knee in motion over last 7 days

End point title	VAS efficacy changes from baseline (Part 1) - treated knee in motion over last 7 days
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

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

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	-36.50 (± 26.837)	-42.50 (± 19.434)	-45.50 (± 7.858)	-44.00 (± 15.716)
Day 30	-54.50 (± 26.725)	-57.25 (± 10.308)	-53.50 (± 16.454)	-43.67 (± 28.937)
Day 90	-57.17 (± 24.609)	-48.75 (± 29.748)	-40.83 (± 14.683)	-41.67 (± 17.010)
Day 180	-59.50 (± 20.573)	-27.25 (± 23.726)	-53.17 (± 18.044)	-37.00 (± 24.269)

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	0 ^[4]	3	
Units: score				
arithmetic mean (standard deviation)				
Day 7	-18.67 (± 26.764)	()	-55.67 (± 23.438)	
Day 30	-26.33 (± 29.738)	()	-53.00 (± 28.792)	
Day 90	-27.00 (± 30.414)	()	-65.33 (± 7.638)	
Day 180	-33.33 (± 23.692)	()	-59.67 (± 7.234)	

Notes:

[4] - Subject withdraw consent

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 1) - treated knee in rest over last 2 days

End point title	VAS efficacy changes from baseline (Part 1) - treated knee in rest over last 2 days
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

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

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	2.67 (± 12.342)	-35.50 (± 21.424)	-45.33 (± 33.005)	-48.67 (± 12.097)
Day 30	-11.17 (± 2.754)	-48.75 (± 13.672)	-46.67 (± 37.072)	-50.33 (± 22.279)
Day 90	-11.50 (± 3.279)	-40.25 (± 26.998)	-23.67 (± 23.861)	-38.67 (± 11.930)
Day 180	-11.83 (± 1.756)	-23.75 (± 35.481)	-46.67 (± 38.501)	-34.00 (± 28.844)

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	0 ^[5]	3	
Units: score				
arithmetic mean (standard deviation)				
Day 7	-31.00 (± 29.309)	()	-50.83 (± 11.295)	
Day 30	-35.00 (± 34.044)	()	-53.17 (± 8.808)	
Day 90	-35.00 (± 38.039)	()	-55.50 (± 6.144)	
Day 180	-38.67 (± 35.501)	()	-52.83 (± 9.878)	

Notes:

[5] - Subject withdraw consent

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 1) - treated knee in rest over last 7 days

End point title	VAS efficacy changes from baseline (Part 1) - treated knee in rest over last 7 days
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

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

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score				
arithmetic mean (standard deviation)				
Day 7	0.50 (± 9.124)	-37.75 (± 16.215)	-33.33 (± 28.042)	-40.67 (± 13.051)
Day 30	-11.50 (± 9.987)	-50.00 (± 8.832)	-43.00 (± 27.622)	-47.33 (± 26.274)
Day 90	-14.50 (± 9.526)	-42.00 (± 27.191)	-24.00 (± 25.120)	-42.00 (± 9.539)
Day 180	-14.17 (± 8.221)	-25.25 (± 36.873)	-43.00 (± 26.211)	-29.67 (± 24.132)

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	0 ^[6]	3	
Units: score				
arithmetic mean (standard deviation)				
Day 7	-26.50 (± 18.296)	()	-53.67 (± 11.504)	
Day 30	-28.17 (± 25.702)	()	-55.67 (± 9.609)	
Day 90	-27.17 (± 28.550)	()	-57.67 (± 8.327)	
Day 180	-31.17 (± 24.761)	()	-54.67 (± 10.970)	

Notes:

[6] - Subject withdraw consent

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 2) - treated knee in motion over last 2 days

End point title	VAS efficacy changes from baseline (Part 2) - treated knee in motion over last 2 days
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

Baseline, 7 days, 30 days, 90 days and 180 days after injection and 60, 120 and 150 days after injection (telephone call with patient)

End point values	MTX-071 Group 1 - second injection	MTX-071 Group 1 - third injection		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: score				
arithmetic mean (standard error)				
Day 7	-21.29 (± 7.730)	-24.00 (± 6.807)		
Day 30	-14.83 (± 11.083)	-20.00 (± 4.041)		
Day 60	-30.71 (± 10.179)	-30.00 (± 5.132)		
Day 90	-31.00 (± 7.859)	-31.67 (± 3.383)		
Day 120	-19.57 (± 11.189)	-25.67 (± 7.839)		
Day 150	-16.14 (± 13.965)	-30.67 (± 4.842)		
Day 180	-27.71 (± 10.122)	-29.33 (± 7.860)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 2) - treated knee in motion over last 7 days

End point title	VAS efficacy changes from baseline (Part 2) - treated knee in motion over last 7 days
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End point description:

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

End point type	Secondary
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End point timeframe:

Baseline, 7 days, 30 days, 90 days and 180 days after injection and 60, 120 and 150 days after injection (telephone call with patient).

End point values	MTX-071 Group 1 - second injection	MTX-071 Group 1 - third injection		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: score				
arithmetic mean (standard error)				

Day 7	-21.14 (± 6.602)	-22.00 (± 7.937)		
Day 30	-19.33 (± 10.362)	-24.67 (± 2.333)		
Day 60	-31.86 (± 9.349)	-28.00 (± 5.859)		
Day 90	-31.00 (± 8.813)	-24.00 (± 10.263)		
Day 120	-18.57 (± 11.406)	-22.00 (± 13.013)		
Day 150	-12.57 (± 15.578)	-29.00 (± 9.074)		
Day 180	-25.86 (± 10.122)	-27.67 (± 11.921)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 2) - treated knee in rest over last 2 days

End point title	VAS efficacy changes from baseline (Part 2) - treated knee in rest over last 2 days
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

"Baseline, 7 days, 30 days, 90 days and 180 days after injection and 60, 120 and 150 days after injection (telephone call with patient).

End point values	MTX-071 Group 1 - second injection	MTX-071 Group 1 - third injection		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: score				
arithmetic mean (standard error)				
Day 7	-19.14 (± 10.347)	-16.33 (± 12.441)		
Day 30	-15.67 (± 12.110)	-9.33 (± 13.679)		
Day 60	-22.43 (± 13.582)	-25.00 (± 15.044)		
Day 90	-29.71 (± 9.138)	-12.67 (± 6.333)		
Day 120	-19.14 (± 12.916)	-22.00 (± 15.588)		
Day 150	-14.43 (± 12.806)	-21.67 (± 14.530)		

Day 180	-25.14 ($\pm$ 11.046)	-21.33 ($\pm$ 13.593)		
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Statistical analyses

No statistical analyses for this end point

Secondary: VAS efficacy changes from baseline (Part 2) - treated knee in rest over last 7 days

End point title	VAS efficacy changes from baseline (Part 2) - treated knee in rest over last 7 days
End point description: The severity of arthritis pain in subject's knee was assessed using a 100-millimeter (mm) VAS ranging from 0 mm = no pain and 100 mm = most severe pain. Higher score indicated more pain. Analysis was performed on ITT population.	
End point type	Secondary
End point timeframe: Baseline, 7 days, 30 days, 90 days and 180 days after injection and 60, 120 and 150 days after injection (telephone call with patient).	

End point values	MTX-071 Group 1 - second injection	MTX-071 Group 1 - third injection		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: score				
arithmetic mean (standard error)				
Day 7	-15.57 ($\pm$ 9.307)	-12.67 ($\pm$ 17.247)		
Day 30	-17.67 ($\pm$ 11.704)	-12.67 ($\pm$ 12.414)		
Day 60	-16.57 ($\pm$ 13.136)	-26.33 ($\pm$ 13.170)		
Day 90	-25.57 ($\pm$ 10.181)	-12.33 ($\pm$ 5.897)		
Day 120	-14.14 ($\pm$ 13.154)	-21.33 ($\pm$ 14.438)		
Day 150	-6.00 ($\pm$ 17.562)	-22.00 ($\pm$ 13.317)		
Day 180	-15.71 ($\pm$ 11.195)	-23.33 ($\pm$ 12.143)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in total WOMAC score versus baseline (Part 1)

End point title	Changes in total WOMAC score versus baseline (Part 1)
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End point description:

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

Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

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

End point values	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)	MTX-071 Group 6 - PA (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	3
Units: score				
arithmetic mean (standard error)				
Day 7	-9.0 (± 5.20)	-22.5 (± 4.33)	-19.0 (± 4.93)	-37.3 (± 6.89)
Day 30	-32.7 (± 8.41)	-25.0 (± 5.20)	-28.0 (± 4.16)	-41.3 (± 17.36)
Day 90	-37.0 (± 9.85)	-15.5 (± 9.04)	-16.0 (± 10.97)	-40.7 (± 9.91)
Day 180	-37.7 (± 10.04)	-7.3 (± 7.42)	-21.3 (± 4.18)	-43.3 (± 10.97)

End point values	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)	MTX-071 Group 4 - (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	0 ^[7]	3	
Units: score				
arithmetic mean (standard error)				
Day 7	-0.3 (± 2.96)	()	-24.0 (± 10.21)	
Day 30	-4.0 (± 2.00)	()	-28.7 (± 6.77)	
Day 90	-14.0 (± 5.57)	()	-28.7 (± 7.45)	
Day 180	-23.0 (± 12.34)	()	-31.3 (± 6.39)	

Notes:

[7] - Subject withdraw consent

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 6 months after injection.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	MTX-071 Group 1 - (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 5 - PA (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 2 - (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 6 - PA (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 3 - (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 7 - PA (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 4 - (Part 1)
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Reporting group description: -

Reporting group title	MTX-071 Group 1 - (Part 2) second injection
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Reporting group description: -

Reporting group title	MTX-071 Group 5 - PA (Part 2) second injection
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Reporting group description: -

Reporting group title	MTX-071 Group 1 - (Part 2) third injection
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Reporting group description: -

Serious adverse events	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MTX-071 Group 6 - PA (Part 1)	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MTX-071 Group 4 - (Part 1)	MTX-071 Group 1 - (Part 2) second injection	MTX-071 Group 5 - PA (Part 2) second injection
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MTX-071 Group 1 - (Part 1)	MTX-071 Group 5 - PA (Part 1)	MTX-071 Group 2 - (Part 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 4 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site joint pain			
subjects affected / exposed	2 / 3 (66.67%)	4 / 4 (100.00%)	2 / 3 (66.67%)
occurrences (all)	1	1	1

Injection site pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Joint stiffness subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain in extremity	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	MTX-071 Group 6 - PA (Part 1)	MTX-071 Group 3 - (Part 1)	MTX-071 Group 7 - PA (Part 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	1 / 1 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Injection site joint pain			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	1 / 1 (100.00%)
occurrences (all)	1	1	1
Injection site pain			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 1 (100.00%) 1
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Nasal congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Joint stiffness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 1 (100.00%) 1
Neck pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0

Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 1 (100.00%) 1
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0
Folliculitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 1 (0.00%) 0

Non-serious adverse events	MTX-071 Group 4 - (Part 1)	MTX-071 Group 1 - (Part 2) second injection	MTX-071 Group 5 - PA (Part 2) second injection
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)	6 / 7 (85.71%)	1 / 1 (100.00%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 1 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1	0 / 7 (0.00%) 0 0 / 7 (0.00%) 0	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0
General disorders and administration site conditions Injection site joint pain subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 1 0 / 3 (0.00%) 0	4 / 7 (57.14%) 1 0 / 7 (0.00%) 0	1 / 1 (100.00%) 1 0 / 1 (0.00%) 0
Gastrointestinal disorders			

Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 1 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 1 (0.00%) 0
Nasal congestion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 7 (42.86%) 1	1 / 1 (100.00%) 1
Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Joint stiffness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 1 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	1 / 1 (100.00%) 1
Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 1 (0.00%) 0
Infections and infestations Bronchitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	MTX-071 Group 1 - (Part 2) third injection		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site joint pain			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Joint stiffness subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		

Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2016	Addition of additional subjects and change of premedication
16 January 2017	Addition of part 2 with repeated dose.
02 February 2018	Change in Principal Investigator, new batches of RTX and buffer for administration of third dose, extension of period of inclusion after the second administration from 9 to 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported