Clinical trial results:
A Multicenter, Long-term, Open-label Study to Evaluate the Safety of MT10109L (NivobotulinumtoxinA) for the Treatment of Glabellar Lines and Lateral Canthal Lines

Summary

EudraCT number	2014-005303-24
Trial protocol	DE BE
Global end of trial date	16 February 2023

Results information

Result version number	v1 (current)
This version publication date	25 September 2024
First version publication date	25 September 2024
Summary attachment (see zip file)	Supplementary Results for Efficacy Endpoints (2014-005303-24_Summary of conclusions for efficacy endpoints.pdf)

Trial information

Trial identification

Sponsor protocol code	MT10109L-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04157686
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 121473

Notes:

Sponsors

Sponsor organisation name	Medytox Inc
Sponsor organisation address	78, Gangni 1-gil, Ochang-eup, Cheongwon-gu, Cheongju-si, Korea, Republic of, 28196
Public contact	Wansoon Lee, Medytox, +82 269015851, drlee@medytox.com
Scientific contact	Wansoon Lee, Medytox, +82 269015851, drlee@medytox.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	09 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2023
Global end of trial reached?	Yes
Global end of trial date	16 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety of repeat treatments of MT10109L in participants with moderate to severe GL, LCL, or both (GL and LCL).

This was a Phase 3, multicenter, open-label, repeat treatment extension study to evaluate the long-term safety of MT10109L in treating Glabellar Lines (GL), Lateral Canthal Lines (LCL), or both (GL and LCL) conducted across 40 global study centers.

All participants who completed studies MT10109L-001 (GL; EudraCT Number: 2018-004384-31), MT10109L-002 (LCL; EudraCT Number: 2014-005279-10), MT10109L-005 (GL with or without LCL; EudraCT Number: 2014-005301-21), and MT10109L-006 (LCL with or without GL; EudraCT Number: 2014-005302-38) were eligible to enroll into this study.

Given the objective of this study was long-term safety, we present the safety-related endpoint data within the full data set. Additionally, we have attached a summary of conclusions page for the efficacy endpoints.

Protection of trial subjects:

The study protocol, all study protocol amendments, written study participant information, informed consent form (ICF), Investigator's Brochure (IB) and any other relevant documents were reviewed and approved by an independent ethics committee (IEC) or institutional review board (IRB) at each study center.

The study was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonization (ICH)/Good Clinical Practice (GCP) and other Guidelines, and applicable laws and regulations.
An ICF approved by each study center's IEC/IRB was signed by the participant or their legally authorized representative and the authorized person obtaining the ICF before the participant was entered in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 October 2019
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	United States: 628
Country: Number of subjects enrolled	Canada: 126
Country: Number of subjects enrolled	Russian Federation: 42

Country: Number of subjects enrolled	United Kingdom: 56
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Germany: 83
Worldwide total number of subjects	957
EEA total number of subjects	105

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)	902
From 65 to 84 years	53
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Approximately 800 participants were planned to be enrolled. A total of 957 participants were enrolled and treated, and 759 participants completed the study. There were 794 participants in the modified intent-to-treat (mITT) population, which were used for the efficacy of EU agencies and 957 pts in ITT population which were used for safety analyze.

Pre-assignment

Screening details:

Study MT10109L-004 is an open-label extension involving participants from MT10109L-001, -002, -005 and -006 (referred to as Lead-In studies).Participants from the lead-in studies, who met the eligibility criteria, were enrolled to continue receiving additional cycles of MT10109L in their respective treatment areas:

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/MT10109L 20U

Arm description:

The participant pool in this arm were from the MT 10109L-001 lead in study (EudraCT Number: 2018-004384-31) who received placebo in period 1 and MT 10109L 20U in period 2. Eligible participants from this study continued receiving 20 U Dose in this open label MT 10109L-004 study.

Arm type	Experimental
Investigational medicinal product name	MT 10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20 U was injected into the GL area.

Arm title	Placebo/MT10109L 24U

Arm description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received Placebo in period 1 and MT10109L 24U in period 2. Eligible participants from this study continued receiving 24 U Dose in the open-label MT10109L-004 study. MT10109L 24 U werel injected into the LCL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 24 U was injected into the LCL area.

Arm title	Placebo/MT10109L 44U

Arm description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and

MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received Placebo in periods 1 & 2. Eligible participants from this study received 20U Dose into the GL area and 24 U Dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U was injected into the GL area plus MT10109L 24U injected into the LCL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20 U was injected into the GL area plus MT10109L 24 U was injected into the LCL area

Arm title	MT10109L 20 U / MT10109L 20 U

Arm description:

The participant pool in this arm were from the MT10109L-001 lead-in study (EudraCT Number: 2018-004384-31), who received MT10109L 20U each in period 1 and period 2. Eligible participants from this study continued receiving Dose 1 in the open-label MT10109L-004 study. MT10109L Dose 1: MT10109L 20U was injected into the GL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20 U was injected into the GL area.

Arm title	MT10109L 24U/MT10109L 24U

Arm description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received MT10109L 24U each in period 1 and period 2. Eligible participants from this study continued receiving 24U dose in this open-label MT10109L-004 study. MT10109L 24 U were injected into the LCL area

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 24 U was injected into the LCL area.

Arm title	MT10109L 20U/MT10109L 44U

Arm description:

The participant pool in this arm were from the from MT10109L-005 lead-in study (EudraCT Number: 2014-005301-21), who received MT10109L 20U in periods 1 and 2. Eligible participants from this study received 20U dose into the GL area and 24U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U were injected into the GL area plus MT10109L 24U were injected into the LCL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20U was injected into the GL area plus MT10109L 24U injected into the LCL area.

Arm title	MT10109L 24U/MT10109L 44U

Arm description:

The participant pool in this arm were from the MT10109L-006 lead-in study (EudraCT Number: 2014-005302-38), who received MT10109L 24U in periods 1 and 2. Eligible participants from this study receives 20 U dose into the GL area and 24 U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U dose injected into the LCL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20 U was injected into the GL area plus MT10109L 24 U was injected into the LCL area.

Arm title	MT10109L 44U /MT10109L 44U

Arm description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received MT10109L 20 U into GL and 24U into LCL in periods 1 & 2. Eligible participants from this study received 20 U Dose into the GL area and 24 U Dose into the LCL area in this open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U injected into the LCL area.

Arm type	Experimental
Investigational medicinal product name	MT10109L
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Sterile concentrate
Routes of administration	Intramuscular use

Dosage and administration details:

MT10109L 20 U was injected into the GL area plus MT10109L 24 U was injected into the LCL area.

Number of subjects in period 1	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U
Started	55	56	118
Completed	43	41	89
Not completed	12	15	29
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	10	10	12
Physician decision	-	-	1
Adverse event, non-fatal	1	-	1
Pregnancy	-	1	3
Other reasons	-	2	4
Lost to follow-up	1	2	8

Protocol deviation	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	MT10109L 20 U / MT10109L 20 U	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U
Started	116	108	128
Completed	87	83	106
Not completed	29	25	22
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	20	12	11
Physician decision	-	1	-
Adverse event, non-fatal	-	1	-
Pregnancy	-	-	-
Other reasons	1	4	6
Lost to follow-up	6	6	3
Protocol deviation	-	1	-
Lack of efficacy	-	-	2

Number of subjects in period 1	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Started	123	253
Completed	92	218
Not completed	31	35
Adverse event, serious fatal	-	-
Consent withdrawn by subject	18	24
Physician decision	3	-
Adverse event, non-fatal	-	-
Pregnancy	3	-
Other reasons	-	1
Lost to follow-up	7	9
Protocol deviation	-	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo/MT10109L 20U

Reporting group description:

The participant pool in this arm were from the MT 10109L-001 lead in study (EudraCT Number: 2018-004384-31) who received placebo in period 1 and MT 10109L 20U in period 2. Eligible participants from this study continued receiving 20 U Dose in this open label MT 10109L-004 study.

Reporting group title	Placebo/MT10109L 24U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received Placebo in period 1 and MT10109L 24U in period 2. Eligible participants from this study continued receiving 24 U Dose in the open-label MT10109L-004 study. MT10109L 24 U werel injected into the LCL area.

Reporting group title	Placebo/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received Placebo in periods 1 & 2. Eligible participants from this study received 20U Dose into the GL area and 24 U Dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U was injected into the GL area plus MT10109L 24U injected into the LCL area.

Reporting group title	MT10109L 20 U / MT10109L 20 U

Reporting group description:

The participant pool in this arm were from the MT10109L-001 lead-in study (EudraCT Number: 2018-004384-31), who received MT10109L 20U each in period 1 and period 2. Eligible participants from this study continued receiving Dose 1 in the open-label MT10109L-004 study. MT10109L Dose 1: MT10109L 20U was injected into the GL area.

Reporting group title	MT10109L 24U/MT10109L 24U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received MT10109L 24U each in period 1 and period 2. Eligible participants from this study continued receiving 24U dose in this open-label MT10109L-004 study. MT10109L 24 U were injected into the LCL area

Reporting group title	MT10109L 20U/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the from MT10109L-005 lead-in study (EudraCT Number: 2014-005301-21), who received MT10109L 20U in periods 1 and 2. Eligible participants from this study received 20U dose into the GL area and 24U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U were injected into the GL area plus MT10109L 24U were injected into the LCL area.

Reporting group title	MT10109L 24U/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-006 lead-in study (EudraCT Number: 2014-005302-38), who received MT10109L 24U in periods 1 and 2. Eligible participants from this study receives 20 U dose into the GL area and 24 U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U dose injected into the LCL area.

Reporting group title	MT10109L 44U /MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received MT10109L 20 U into GL and 24U into LCL in periods 1 & 2. Eligible participants from this study received 20 U Dose into the GL area and 24 U Dose into the LCL area in this open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U injected into the LCL area.

Reporting group values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U
Number of subjects	55	56	118
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	54	54	110
From 65-84 years	1	2	7
85 years and over	0	0	1
Age continuous			
Units: years			
arithmetic mean	47.1	46.7	48.2
standard deviation	± 10.18	± 11.75	± 11.68
Gender categorical			
Units: Subjects			
Female	53	42	99
Male	2	14	19

Reporting group values	MT10109L 20 U / MT10109L 20 U	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U
Number of subjects	116	108	128
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	107	103	120
From 65-84 years	9	5	7
85 years and over	0	0	1
Age continuous			
Units: years			
arithmetic mean	46.9	47.1	47.8
standard deviation	± 12.17	± 10.34	± 11.24
Gender categorical			
Units: Subjects			
Female	106	87	109
Male	10	21	19

Reporting group values	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U	Total
Number of subjects	123	253	957

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	113	241	902
From 65-84 years	10	12	53
85 years and over	0	0	2
Age continuous Units: years			
arithmetic mean	48.5	47.9	
standard deviation	± 10.53	± 10.80	-
Gender categorical Units: Subjects			
Female	103	227	826
Male	20	26	131

Subject analysis sets

Subject analysis set title	Demographic and other Baseline Characteristics - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants from prior Phase 3 studies were enrolled in this study as follows: 171 participants from -001 study, 164 participants from -002 study, 303 participants from -005 study, and 319 participants from -006 study; thus, consisting of 957 participants in the ITT analysis set.

Subject analysis set title	Demographic and other Baseline Characteristics -mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants from prior Phase 3 study were enrolled in this study as follows: 142 participants from 001 study, 127 participants from 002 study, 255 participants from 005 study, and 270 participants from 006 study; thus, consisting of 794 participants in the mITT analysis set.

Reporting group values	Demographic and other Baseline Characteristics - ITT	Demographic and other Baseline Characteristics - mITT	
Number of subjects	957	794	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	902	746	
From 65-84 years	53	46	
85 years and over	2	2	

Age continuous Units: years			
arithmetic mean	47.7	48.6	
standard deviation	± 11.06	± 10.65	
Gender categorical Units: Subjects			
Female	826	705	
Male	131	89	

End points

End points reporting groups

Reporting group title	Placebo/MT10109L 20U

Reporting group description:

The participant pool in this arm were from the MT 10109L-001 lead in study (EudraCT Number: 2018-004384-31) who received placebo in period 1 and MT 10109L 20U in period 2. Eligible participants from this study continued receiving 20 U Dose in this open label MT 10109L-004 study.

Reporting group title	Placebo/MT10109L 24U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received Placebo in period 1 and MT10109L 24U in period 2. Eligible participants from this study continued receiving 24 U Dose in the open-label MT10109L-004 study. MT10109L 24 U werel injected into the LCL area.

Reporting group title	Placebo/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received Placebo in periods 1 & 2. Eligible participants from this study received 20U Dose into the GL area and 24 U Dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U was injected into the GL area plus MT10109L 24U injected into the LCL area.

Reporting group title	MT10109L 20 U / MT10109L 20 U

Reporting group description:

The participant pool in this arm were from the MT10109L-001 lead-in study (EudraCT Number: 2018-004384-31), who received MT10109L 20U each in period 1 and period 2. Eligible participants from this study continued receiving Dose 1 in the open-label MT10109L-004 study. MT10109L Dose 1: MT10109L 20U was injected into the GL area.

Reporting group title	MT10109L 24U/MT10109L 24U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study (EudraCT Number: 2014-005279-10), who received MT10109L 24U each in period 1 and period 2. Eligible participants from this study continued receiving 24U dose in this open-label MT10109L-004 study. MT10109L 24 U were injected into the LCL area

Reporting group title	MT10109L 20U/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the from MT10109L-005 lead-in study (EudraCT Number: 2014-005301-21), who received MT10109L 20U in periods 1 and 2. Eligible participants from this study received 20U dose into the GL area and 24U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20U were injected into the GL area plus MT10109L 24U were injected into the LCL area.

Reporting group title	MT10109L 24U/MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-006 lead-in study (EudraCT Number: 2014-005302-38), who received MT10109L 24U in periods 1 and 2. Eligible participants from this study receives 20 U dose into the GL area and 24 U dose into the LCL area in the open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U dose injected into the LCL area.

Reporting group title	MT10109L 44U /MT10109L 44U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 (EudraCT Number: 2014-005301-21) and MT10109L-006 (EudraCT Number: 2014-005302-38) lead-in studies, who received MT10109L 20 U into GL and 24U into LCL in periods 1 & 2. Eligible participants from this study received 20 U Dose into the GL area and 24 U Dose into the LCL area in this open-label MT10109L-004 study. MT10109L 20 U were injected into the GL area plus MT10109L 24 U injected into the LCL area.

Subject analysis set title	Demographic and other Baseline Characteristics - ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants from prior Phase 3 studies were enrolled in this study as follows: 171 participants from -001

study, 164 participants from -002 study, 303 participants from -005 study, and 319 participants from -006 study; thus, consisting of 957 participants in the ITT analysis set.

Subject analysis set title	Demographic and other Baseline Characteristics -mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants from prior Phase 3 study were enrolled in this study as follows: 142 participants from 001 study, 127 participants from 002 study, 255 participants from 005 study, and 270 participants from 006 study; thus, consisting of 794 participants in the mITT analysis set.

Primary: Number of Participants Who Experienced Any Adverse Event (AE)

End point title	Number of Participants Who Experienced Any Adverse Event (AE)[1]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

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: Data has only been summarized as frequency of events per arm. No statistical comparisons were made between the arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	56	118	116
Units: number of participants	39	39	80	89

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	128	123	253
Units: number of participants	74	80	89	183

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced Treatment-Related Adverse Events (TEAEs)

End point title	Number of Participants Who Experienced Treatment-Related Adverse Events (TEAEs)[2]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study exit

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: Data has only been summarized as frequency of events per arm. No statistical comparisons were made between the arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	56	118	116
Units: Number of Participants	18	4	31	34

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	128	123	253
Units: Number of Participants	11	22	42	73

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Pulse Rate (Beats Per Minute)

End point title	Mean Change From Baseline in Pulse Rate (Beats Per Minute)[3]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

Notes:

[3] - 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: Only descriptive statistics were used to summarize the mean changes from vital signs from baseline. No statistical comparisons were made between arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	40	63	58
Units: beats/min				
arithmetic mean (standard deviation)	3.2 (± 15.01)	-2.2 (± 13.35)	-1.2 (± 10.95)	2.0 (± 12.77)

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	78	74	157
Units: beats/min				
arithmetic mean (standard deviation)	0.6 (± 11.58)	0.7 (± 10.97)	3.0 (± 10.34)	1.0 (± 8.93)

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Systolic Blood Pressure (mm Hg)

End point title	Mean Change From Baseline in Systolic Blood Pressure (mm Hg)[4]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

Notes:

[4] - 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: Only descriptive statistics were used to summarize the mean changes from vital signs from baseline. No statistical comparisons were made between arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	40	63	58
Units: mm Hg				
arithmetic mean (standard deviation)	1.4 (± 12.59)	-1.9 (± 10.44)	1.9 (± 14.44)	0.6 (± 16.72)

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	78	74	157
Units: mm Hg				
arithmetic mean (standard deviation)	1.1 (± 13.84)	1.8 (± 15.24)	1.4 (± 14.17)	-0.4 (± 13.83)

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Diastolic Blood Pressure (mm Hg)

End point title	Mean Change From Baseline in Diastolic Blood Pressure (mm Hg)[5]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

Notes:

[5] - 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: Only descriptive statistics were used to summarize the mean changes from vital signs from baseline. No statistical comparisons were made between arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	40	63	58
Units: mm Hg				
arithmetic mean (standard deviation)	1.1 (± 11.3)	-0.6 (± 11.74)	1.3 (± 9.61)	1.5 (± 11.68)

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	78	74	157
Units: mm Hg				
arithmetic mean (standard deviation)	0.7 (± 7.57)	0.0 (± 10.62)	2.3 (± 9.53)	-0.3 (± 9.46)

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in Respiratory Rate (Breaths Per Minute)

End point title	Mean Change From Baseline in Respiratory Rate (Breaths Per Minute)[6]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

Notes:

[6] - 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: Only descriptive statistics were used to summarize the mean changes from vital signs from baseline. No statistical comparisons were made between arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	40	63	58
Units: breath/min				
arithmetic mean (standard deviation)	0.3 (± 2.09)	0.6 (± 2.15)	-0.5 (± 1.92)	0.2 (± 2.78)

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	78	74	157
Units: breath/min				
arithmetic mean (standard deviation)	0.5 (± 1.94)	-0.4 (± 2.29)	0.4 (± 2.21)	-0.1 (± 2.3)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Binding and Neutralizing Antibodies

End point title	Number of Participants With Binding and Neutralizing Antibodies[7]

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 720 or Study Exit

Notes:

[7] - 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: Only descriptive statistics were used to summarize the mean changes from vital signs from baseline. No statistical comparisons were made between arms.

End point values	Placebo/MT10109L 20U	Placebo/MT10109L 24U	Placebo/MT10109L 44U	MT10109L 20 U / MT10109L 20 U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	56	118	116
Units: Number of Participant	0	0	0	0

End point values	MT10109L 24U/MT10109L 24U	MT10109L 20U/MT10109L 44U	MT10109L 24U/MT10109L 44U	MT10109L 44U /MT10109L 44U
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	128	123	253
Units: Number of Participant	2	0	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The safety analyses were conducted in the Intent-to-Treat (ITT) population. All adverse events were collected from the signing of the ICF to 30 days after the participant's last study visit. Unless otherwise noted, safety results refer to TEAEs.

Adverse event reporting additional description:

Treatment-Emergent Adverse Events (TEAEs)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo/MT10109L 20 U

Reporting group description:

The participant pool in this arm were from the MT10109L-001 lead-in study, who received Placebo in period 1 and MT10109L 20 U in period 2 in the GL area.

Eligible participants from this study received 20 U in GL area in the open-label MT10109L-004 study.

Reporting group title	Placebo/MT10109L 24 U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study, who received Placebo in period 1 and MT10109L 24 U in period 2.

Eligible participants from this study continued receiving 24 U in the LCL area in the open-label MT10109L-004 study.

Reporting group title	Placebo/MT10109L 44 U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 and MT10109L-006 lead-in studies, who received Placebo in periods 1 & 2 in the GL and LCL areas.

Eligible participants from this study received 20 U into the GL area and 24 U into the LCL area in the open-label MT10109L-004 study.

Reporting group title	MT10109L 20 U/20 U

Reporting group description:

The participant pool in this arm were from the MT10109L-001 lead-in study, who received MT10109L 20 U each in period 1 and period 2 in the GL area.

Eligible participants from this study continued receiving 20 in the GL area in the open-label MT10109L-004 study.

Reporting group title	MT10109L 24 U/24 U

Reporting group description:

The participant pool in this arm were from the MT10109L-002 lead-in study, who received MT10109L 24 U each in period 1 and period 2 in the LCL area.

Eligible participants from this study continued receiving 24 U in the LCL area in the open-label MT10109L-004 study.

Reporting group title	MT10109L 20 U/44 U

Reporting group description:

The participant pool in this arm were from the from MT10109L-005 lead-in study, who received MT10109L 20 U in periods 1 and 2.

Eligible participants from this study received 20 U into the GL area and 24 U into the LCL area in the open-label MT10109L-004 study.

Reporting group title	MT10109L 24 U/44 U

Reporting group description:

The participant pool in this arm were from the MT10109L-006 lead-in study, who received MT10109L 24 U in the LCL area in periods 1 and 2.

Eligible participants from this study continued to receive 20 U into the GL area and 24 U into the LCL area in the open-label MT10109L-004 study.

Reporting group title	MT10109L 44 U/44 U

Reporting group description:

The participant pool in this arm were from the MT10109L-005 and MT10109L-006 lead-in studies, who received MT10109L 20 U into GL and 24 U into LCL in periods 1 & 2.

Eligible participants from this study continued to receive 20 U into the GL area and 24 U into the LCL area in the open-label MT10109L-004 study.

Serious adverse events	Placebo/MT10109L 20 U	Placebo/MT10109L 24 U	Placebo/MT10109L 44 U
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 55 (5.45%)	1 / 56 (1.79%)	10 / 118 (8.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	2 / 118 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basosquamous carcinoma A			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer stage I			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Hormone receptor positive breast cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Malignant melanoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Malignant melanoma in situ			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 118 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Plasma cell myeloma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Renal cell carcinoma			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 55 (0.00%)	1 / 56 (1.79%)	0 / 118 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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			
Abortion induced			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod sting			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Fall			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Hip fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Intentional overdose			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 118 (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
Radius fracture			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 118 (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
Road traffic accident			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	0 / 118 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Tachycardia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Facial paralysis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Syncope			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Cholelithiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Exostosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Osteoarthritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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			
Appendicitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID 19			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
COVID 19 Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Diverticulitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Endometritis			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Perirectal abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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
Obesity			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	0 / 118 (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	MT10109L 20 U/20 U	MT10109L 24 U/24 U	MT10109L 20 U/44 U
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 116 (6.90%)	9 / 108 (8.33%)	7 / 128 (5.47%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			

subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basosquamous carcinoma A			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Bone cancer			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Breast cancer stage I			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Hormone receptor positive breast cancer			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Malignant melanoma			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Malignant melanoma in situ			

subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Plasma cell myeloma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Rectal cancer			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Renal cell carcinoma			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Uterine leiomyoma			

subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
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			
Acute respiratory failure			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Depression			

subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Face injury			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Fall			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Hip fracture			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Intentional overdose			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Radius fracture			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Road traffic accident			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Facial paralysis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Cholelithiasis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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			
Arthritis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Exostosis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Osteoarthritis			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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

COVID 19			
subjects affected / exposed	1 / 116 (0.86%)	1 / 108 (0.93%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
COVID 19 Pneumonia			
subjects affected / exposed	2 / 116 (1.72%)	1 / 108 (0.93%)	2 / 128 (1.56%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Perirectal abscess			
subjects affected / exposed	1 / 116 (0.86%)	0 / 108 (0.00%)	0 / 128 (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
Pneumonia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 108 (0.00%)	0 / 128 (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
Obesity			

subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	0 / 128 (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

Serious adverse events	MT10109L 24 U/44 U	MT10109L 44 U/44 U	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 123 (10.57%)	13 / 253 (5.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	3 / 123 (2.44%)	3 / 253 (1.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma A			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer stage I			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hormone receptor positive breast cancer			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 123 (0.81%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (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			
Abortion induced			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	2 / 123 (1.63%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 123 (0.81%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (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			
Arthritis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (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			
Appendicitis			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID 19			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID 19 Pneumonia			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			

subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 123 (0.00%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 123 (0.81%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 123 (0.00%)	1 / 253 (0.40%)	
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	Placebo/MT10109L 20 U	Placebo/MT10109L 24 U	Placebo/MT10109L 44 U
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 55 (47.27%)	23 / 56 (41.07%)	58 / 118 (49.15%)
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 56 (0.00%)	1 / 118 (0.85%)
occurrences (all)	3	0	1
Procedural pain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 56 (0.00%)	0 / 118 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			

Hypertension			
subjects affected / exposed	4 / 55 (7.27%)	2 / 56 (3.57%)	3 / 118 (2.54%)
occurrences (all)	4	2	3
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 55 (21.82%)	1 / 56 (1.79%)	11 / 118 (9.32%)
occurrences (all)	12	1	11
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	8 / 118 (6.78%)
occurrences (all)	0	0	8
Injection site haemorrhage			
subjects affected / exposed	1 / 55 (1.82%)	3 / 56 (5.36%)	8 / 118 (6.78%)
occurrences (all)	1	3	8
Injection site pain			
subjects affected / exposed	8 / 55 (14.55%)	0 / 56 (0.00%)	10 / 118 (8.47%)
occurrences (all)	8	0	10
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 56 (0.00%)	6 / 118 (5.08%)
occurrences (all)	1	0	6
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 55 (12.73%)	12 / 56 (21.43%)	22 / 118 (18.64%)
occurrences (all)	7	12	22
Influenza			
subjects affected / exposed	2 / 55 (3.64%)	0 / 56 (0.00%)	6 / 118 (5.08%)
occurrences (all)	2	0	6
Nasopharyngitis			
subjects affected / exposed	6 / 55 (10.91%)	4 / 56 (7.14%)	15 / 118 (12.71%)
occurrences (all)	6	4	15
Sinusitis			
subjects affected / exposed	2 / 55 (3.64%)	5 / 56 (8.93%)	4 / 118 (3.39%)
occurrences (all)	2	5	4
Upper respiratory tract infection			

subjects affected / exposed	0 / 55 (0.00%)	0 / 56 (0.00%)	11 / 118 (9.32%)
occurrences (all)	0	0	11

Non-serious adverse events	MT10109L 20 U/20 U	MT10109L 24 U/24 U	MT10109L 20 U/44 U
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 116 (46.55%)	45 / 108 (41.67%)	50 / 128 (39.06%)
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	3 / 116 (2.59%)	1 / 108 (0.93%)	0 / 128 (0.00%)
occurrences (all)	3	1	0
Procedural pain			
subjects affected / exposed	3 / 116 (2.59%)	0 / 108 (0.00%)	0 / 128 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 116 (4.31%)	3 / 108 (2.78%)	3 / 128 (2.34%)
occurrences (all)	5	3	3
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 116 (10.34%)	5 / 108 (4.63%)	13 / 128 (10.16%)
occurrences (all)	12	5	13
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	3 / 116 (2.59%)	0 / 108 (0.00%)	4 / 128 (3.13%)
occurrences (all)	3	0	4
Injection site haemorrhage			
subjects affected / exposed	0 / 116 (0.00%)	6 / 108 (5.56%)	2 / 128 (1.56%)
occurrences (all)	0	6	2
Injection site pain			
subjects affected / exposed	17 / 116 (14.66%)	0 / 108 (0.00%)	8 / 128 (6.25%)
occurrences (all)	17	0	8
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 116 (1.72%)	2 / 108 (1.85%)	3 / 128 (2.34%)
occurrences (all)	2	2	3
Infections and infestations			

COVID-19			
subjects affected / exposed	18 / 116 (15.52%)	31 / 108 (28.70%)	20 / 128 (15.63%)
occurrences (all)	18	31	20
Influenza			
subjects affected / exposed	0 / 116 (0.00%)	1 / 108 (0.93%)	2 / 128 (1.56%)
occurrences (all)	0	1	2
Nasopharyngitis			
subjects affected / exposed	9 / 116 (7.76%)	8 / 108 (7.41%)	9 / 128 (7.03%)
occurrences (all)	9	8	9
Sinusitis			
subjects affected / exposed	3 / 116 (2.59%)	4 / 108 (3.70%)	3 / 128 (2.34%)
occurrences (all)	3	4	3
Upper respiratory tract infection			
subjects affected / exposed	6 / 116 (5.17%)	5 / 108 (4.63%)	7 / 128 (5.47%)
occurrences (all)	6	5	7

Non-serious adverse events	MT10109L 24 U/44 U	MT10109L 44 U/44 U	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 123 (48.78%)	128 / 253 (50.59%)	
Injury, poisoning and procedural complications			
Ligament Sprain			
subjects affected / exposed	3 / 123 (2.44%)	3 / 253 (1.19%)	
occurrences (all)	3	3	
Procedural pain			
subjects affected / exposed	4 / 123 (3.25%)	2 / 253 (0.79%)	
occurrences (all)	4	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 123 (4.88%)	9 / 253 (3.56%)	
occurrences (all)	6	9	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 123 (10.57%)	27 / 253 (10.67%)	
occurrences (all)	13	27	
General disorders and administration site conditions			

Injection site bruising			
subjects affected / exposed	12 / 123 (9.76%)	20 / 253 (7.91%)	
occurrences (all)	12	20	
Injection site haemorrhage			
subjects affected / exposed	7 / 123 (5.69%)	11 / 253 (4.35%)	
occurrences (all)	7	11	
Injection site pain			
subjects affected / exposed	17 / 123 (13.82%)	23 / 253 (9.09%)	
occurrences (all)	17	23	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 123 (3.25%)	5 / 253 (1.98%)	
occurrences (all)	4	5	
Infections and infestations			
COVID-19			
subjects affected / exposed	22 / 123 (17.89%)	47 / 253 (18.58%)	
occurrences (all)	22	47	
Influenza			
subjects affected / exposed	1 / 123 (0.81%)	1 / 253 (0.40%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	17 / 123 (13.82%)	31 / 253 (12.25%)	
occurrences (all)	17	31	
Sinusitis			
subjects affected / exposed	3 / 123 (2.44%)	7 / 253 (2.77%)	
occurrences (all)	3	7	
Upper respiratory tract infection			
subjects affected / exposed	5 / 123 (4.07%)	15 / 253 (5.93%)	
occurrences (all)	5	15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2019	Substantial Changes: Changes were made to integrate feedback and recommendations from health authorities for the lead-in Phase 3 studies and improve clarity of study processes
31 October 2019	Substantial Changes: The overall rationale for the changes implemented in this open-label, extension study was to integrate feedback and recommendations received from health authorities to date on the lead-in studies.
31 March 2020	EU Specific Amendment 1: The overall rationale for the changes implemented in this open-label, extension study was to integrate feedback and recommendations received from health authorities.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported