Clinical trial results:
A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Evaluate the Safety and Efficacy of MT10109L (NivobotulinumtoxinA) for the Treatment of Lateral Canthal Lines

Summary

EudraCT number	2014-005279-10
Trial protocol	GB
Global end of trial date	25 January 2021

Results information

Result version number	v1 (current)
This version publication date	28 December 2023
First version publication date	28 December 2023

Trial information

Trial identification

Sponsor protocol code	MT10109L-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03785145
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, 28126
Public contact	Young Ryu, Medytox Inc., 82 2-6901-5424,
Scientific contact	Gyungjin Heo, Medytox Inc., 82 2-6901-5839, gjheo@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	29 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2020
Global end of trial reached?	Yes
Global end of trial date	25 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy between MT10109L and placebo for the treatment of lateral canthal Lines (LCL). The total global enrollment (as presented in the "Population of Trial Subjects" below was 235, which included the Intent-To-Treat population. However, all primary and secondary efficacy analyses for EU regulatory endpoints reported here are using the mITT population that included a total of 181 participants (USA -138 ; Russia -9 and; United-Kingdom -34).

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 Harmonisation (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	20 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 45
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	United States: 167
Worldwide total number of subjects	235
EEA total number of subjects	0

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)	224
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were screened and recruited at sites in US, UK and Russia. The data described here is for the Intent-to-Treat population. The Intent-to-treat (ITT) population consisted of all randomized participants.

Pre-assignment

Screening details:

235 met the inclusion/exclusion criteria and were randomized. 234 participants entered the study and were treated.

Period 1

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

Blinding implementation details:

Randomization and double-blinding were used to minimize bias arising from the assignment of participants to treatment groups and the expectations of participants, investigators, and individuals collecting data.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1

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

Dosage and administration details:

6 injection sites. 0.1 ml per injection. Placebo - 0 U per 0.1 ml

Arm title	MT10109L

Arm description:

MT10109L was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1

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

Dosage and administration details:

6 injection sites. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 24 U

Number of subjects in period 1	Placebo	MT10109L
Started	77	158
Completed	68	145
Not completed	9	13
Adverse event, serious fatal	-	1
Consent withdrawn by subject	6	9
Adverse event, non-fatal	-	1
Lost to follow-up	2	2
No injection received	1	-

Period 2

Period 2 title	Open-label - Re- Treatment 1
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MT10109L re-treatment 1 for Placebo arm

Arm description:

In the open-label part, participants who met a protocol-defined retreatment criteria were allowed up to 2 MT10109L injections.

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:

2 treatment cycles in the open-label period. 6 injection sites. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 24 U per treatment cycle

Arm title	MT10109L re-treatment 1 for experimental arm in cycle 1

Arm description:

Participants who met protocol-defined retreatment criteria were eligible to receive up to 2 additional MT10109L injections during the open-label part.

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:

Retreatment cycle in the open-label period. 6 injection sites per treatment. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 24 U per treatment cycle.

Number of subjects in period 2[1]	MT10109L re-treatment 1 for Placebo arm	MT10109L re-treatment 1 for experimental arm in cycle 1
Started	65	144
Completed	61	130
Not completed	4	14
Consent withdrawn by subject	1	5
COVID-19, Enrolled in a different study	2	3
Lost to follow-up	1	6

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only participants from the previous treatment period who met a protocol-defined re-treatment criteria entered into the next treatment period.

Period 3

Period 3 title	Open-label - Re-Treatment 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MT10109L re-treatment 2 for Placebo arm

Arm description:

In the open-label part, participants in the placebo arm who met retreatment criteria were allowed up to 2 MT10109L treatments.

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:

Retreatment cycle in the open-label period. 6 injection sites per treatment. 0.1 ml per injection. Placebo - 4 U per 0.1 ml. Total = 24 U per treatment cycle

Arm title	MT10109L re-treatment 2 for experimental arm

Arm description:

Participants from the experimental arm of period 1 who met protocol-defined retreatment criteria were eligible to receive up to 2 MT10109L during the open-label part.

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:

Retreatment cycle in the open-label period. 6 injection sites per treatment. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 24 U per treatment cycle

Number of subjects in period 3[2]	MT10109L re-treatment 2 for Placebo arm	MT10109L re-treatment 2 for experimental arm
Started	49	91
Completed	49	88
Not completed	0	3
Consent withdrawn by subject	-	1
COVID 19	-	1
Lost to follow-up	-	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only participants from the previous treatment period who met a protocol-defined re-treatment criteria entered into the next treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1	
Reporting group title	MT10109L
Reporting group description:	
MT10109L was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1	

Reporting group values	Placebo	MT10109L	Total
Number of subjects	77	158	235
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)	75	149	224
From 65-84 years	2	9	11
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	46.1	46.6	
standard deviation	± 11.09	± 11.43	-
Gender categorical Units: Subjects			
Female	61	127	188
Male	16	31	47

Subject analysis sets	
Subject analysis set title	Demographic and other Baseline Characteristics - ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
235 participants were included in the Intent-To-Treat (ITT) population (77 participants in the placebo group and 158 participants in the MT10109L group).	
Subject analysis set title	Demographic and other Baseline Characteristics - mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
181 participants were included in the modified Intent To Treat (mITT) population (57 participants in the placebo group and 124 participants in the MT10109L group).	

Reporting group values	Demographic and other Baseline Characteristics - ITT	Demographic and other Baseline Characteristics - mITT	
Number of subjects	235	181	
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)	224	172	
From 65-84 years	11	9	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	46.4	48.0	
standard deviation	± 11.30	± 10.8	
Gender categorical Units: Subjects			
Female	188	152	
Male	47	29	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1	
Reporting group title	MT10109L
Reporting group description:	
MT10109L was injected into the Lateral Canthal Lines (LCL): initial double-blind treatment on Day 1	
Reporting group title	MT10109L re-treatment 1 for Placebo arm
Reporting group description:	
In the open-label part, participants who met a protocol-defined retreatment criteria were allowed up to 2 MT10109L injections.	
Reporting group title	MT10109L re-treatment 1 for experimental arm in cycle 1
Reporting group description:	
Participants who met protocol-defined retreatment criteria were eligible to receive up to 2 additional MT10109L injections during the open-label part.	
Reporting group title	MT10109L re-treatment 2 for Placebo arm
Reporting group description:	
In the open-label part, participants in the placebo arm who met retreatment criteria were allowed up to 2 MT10109L treatments.	
Reporting group title	MT10109L re-treatment 2 for experimental arm
Reporting group description:	
Participants from the experimental arm of period 1 who met protocol-defined retreatment criteria were eligible to receive up to 2 MT10109L during the open-label part.	
Subject analysis set title	Demographic and other Baseline Characteristics - ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
235 participants were included in the Intent-To-Treat (ITT) population (77 participants in the placebo group and 158 participants in the MT10109L group).	
Subject analysis set title	Demographic and other Baseline Characteristics - mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
181 participants were included in the modified Intent To Treat (mITT) population (57 participants in the placebo group and 124 participants in the MT10109L group).	

Primary: Co-Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Investigator Assessment of LCL Severity at Maximum Smile at Day 30 of Treatment Cycle 1

End point title	Co-Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Investigator Assessment of LCL Severity at Maximum Smile at Day 30 of Treatment Cycle 1
End point description:	
All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50. The data presents the percentage of participants who had LCL severity at maximum smile of none or mild based on investigator FWS rating at cycle 1 day 30. FWS is a 4-point grading scale where 0=none, 1=mild, 2=moderate, 3=severe	
End point type	Primary
End point timeframe:	
Day 30	

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	124		
Units: Participants	4	78		

Statistical analyses

Statistical analysis title	% of Participants Achieving None or Mild on FWS

Statistical analysis description:

All primary and secondary efficacy analyses endpoints were carried out using the modified Intent-To-Treat (mITT) population which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50. Multiple imputation method was used for missing variables in primary efficacy endpoint. Analyses of the secondary efficacy variables were performed using observed data.

Comparison groups	Placebo v MT10109L
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Notes:

[1] - The equality of the proportions of responders was analyzed using the CMH tests stratified by LCL baseline severity.

Primary: Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Participant Assessment of LCL Severity at Maximum Smile at Day 30 of Treatment Cycle 1

End point title	Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Participant Assessment of LCL Severity at Maximum Smile at Day 30 of Treatment Cycle 1

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The data here presents the percentage of participants who had LCL severity at maximum smile of none or mild based on participant FWS rating at Cycle 1 Day 30.
FWS is 4-point grading scale, where 0=none, 1=mild, 2=moderate, and 3=severe.

End point type	Primary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	124		
Units: Participants	3	70		

Statistical analyses

Statistical analysis title	% of Participants achieving primary endpoint

Statistical analysis description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50. Multiple imputation method was used for missing variables in primary efficacy endpoint.

Comparison groups	Placebo v MT10109L
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel

Notes:

[2] - The equality of the proportions of responders was analyzed using the CMH tests stratified by LCL baseline severity.

Secondary: Secondary 1: The duration of LCL treatment effect estimated as the median time to return to moderate or severe LCL at maximum smile in participants who achieved a rating of none or mild LCL severity at maximum smile at Day 30

End point title	Secondary 1: The duration of LCL treatment effect estimated as the median time to return to moderate or severe LCL at maximum smile in participants who achieved a rating of none or mild LCL severity at maximum smile at Day 30

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The investigator evaluates the participant's LCL severity using a 4-grade FWS scale (0 to 3) where 0=none and 3 = severe. The outcome is measured as median time to loss of treatment effect (i.e., return to moderate or severe LCL severity at maximum smile using the FWS).
FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	71		
Units: Days				
median (inter-quartile range (Q1-Q3))	113.0 (57.0 to 157.0)	117.5 (85.0 to 158.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 2: The percentage of participants reporting mostly satisfied/very satisfied on a 5-point scale of very dissatisfied to very satisfied on the FLSQ follow-up version Item 5 for LCL at Day 60

End point title	Secondary 2: The percentage of participants reporting mostly satisfied/very satisfied on a 5-point scale of very dissatisfied to very satisfied on the FLSQ follow-up version Item 5 for LCL at Day 60

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.

The Satisfaction Question 5, grades facial line treatment satisfaction on a 5-point scale (-2 to 2) where -2=Very dissatisfied and 2=Very satisfied.

End point type	Secondary

End point timeframe:

Day 60

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	105		
Units: Participants	1	81		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 3 The percentage of responders for investigator assessments of LCL severity at rest using the FWS among participants who were rated at least mild at rest at baseline, where a responder is defined as achieving a ≥ 1-grade improvement at Day 30

End point title	Secondary 3 The percentage of responders for investigator assessments of LCL severity at rest using the FWS among participants who were rated at least mild at rest at baseline, where a responder is defined as achieving a ≥ 1-grade improvement at Day 30

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.

The percentage of participants who achieved a ≥1-grade improvement from baseline LCL severity at rest based on investigator FWS rating is presented here.
FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	109		
Units: Participants	5	57		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 4: The percentage of responders for participant assessments of LCL severity at rest using the FWS among participants who were rated at least mild at rest at baseline, where a responder was defined as achieving a ≥ 1-grade improvement at Day 30

End point title	Secondary 4: The percentage of responders for participant assessments of LCL severity at rest using the FWS among participants who were rated at least mild at rest at baseline, where a responder was defined as achieving a ≥ 1-grade improvement at Day 30

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The percentage of participants who achieved a ≥1-grade improvement from baseline LCL severity at rest based on participants FWS rating is presented here.
FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	112		
Units: Participants	13	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 5 The percentage of participants with a ≥ 20-point improvement from baseline at Day 30 on the 11-Item Facial Line Outcomes (FLO-11) Questionnaire total score for LCL

End point title	Secondary 5 The percentage of participants with a ≥ 20-point improvement from baseline at Day 30 on the 11-Item Facial Line Outcomes (FLO-11) Questionnaire total score for LCL

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The percentage of participants who achieved a ≥20-point improvement from baseline on the FLSQ impact domain (eg, reported a good improvement of the facial lines negative impact)
are presented here.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	116		
Units: Participants	8	75		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 6: The percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 2 for LCL

End point title	Secondary 6: The percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 2 for LCL

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The percentage of participants who achieved a ≥4-point improvement from baseline on the FLO-11 questionnaire item 2 for LCL (eg, reported good improvement in the appearance of skin age) is presented
here.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	116		
Units: Participants	4	56		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 7: The percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 5 for LCL

End point title	Secondary 7: The percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 5 for LCL

End point description:

All primary and secondary efficacy analyses for EU regulatory endpoints were carried out using the mITT population, which consisted of all randomized participants who had a baseline transformed FLO-11 questionnaire total score of ≤50.
The percentage of participants who achieved a ≥4-point improvement from baseline on the FLO-11 questionnaire item 5 for LCL (eg, reported good improvement in attractiveness) is presented here.

End point type	Secondary

End point timeframe:

Day 30

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	114		
Units: Participants	5	55		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The time frame for AEs is from the first dose on Day 1 and up to 30 days after their last visit or study exit (Day 360 or early exit).

Adverse event reporting additional description:

All safety analyses were carried out using the Safety population, defined as pcts who received at least 1 dose of study intervention. All safety analyses were performed with pcts analyzed by their actual treatment or regimen received. Placebo pcts who entered open-label phase (post Day 180) and received study intervention are counted in MT10109L gp

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	MT10109L

Reporting group description:

MT10109L was injected into the LCL: initial double-blind treatment on Day 1, and up to 2 open-label study interventions during the retreatment period. Placebo participants who experienced TEAE after receiving MT10109L during open-label phase were counted here.

Reporting group title	Placebo

Reporting group description:

Placebo was injected into the LCL: initial double-blind treatment on Day 1. In the openlabel period (post day 180), up to 2 MT10109L treatments were possible. TEAEs with onset date after the MT10109L treatment were not counted here.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Non-serious adverse events recorded were below the threshold of 5%.

Serious adverse events	MT10109L	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 223 (3.14%)	0 / 76 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			

Alcohol poisoning			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Exostosis			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Suspected COVID-19			
subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 223 (0.45%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	MT10109L	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 223 (0.00%)	0 / 76 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2019	The primary purpose of this protocol amendment was to integrate feedback and recommendations from health authorities and improve clarity of study processes. This amendment is considered substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported