



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 With or Without Concurrent Treatment of Glabellar Lines

Summary

EudraCT number	2014-005302-38
Trial protocol	DE
Global end of trial date	25 January 2021

Results information

Result version number	v1 (current)
This version publication date	18 January 2024
First version publication date	18 January 2024

Trial information

Trial identification

Sponsor protocol code	MT10109L-006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03732833
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 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	05 March 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 24 U MT10109L and placebo for the treatment of LCL (with or without concurrent 20 U treatment of GL) in participants with moderate to severe LCL and GL.

The total global enrollment (as presented in the "Population of Trial Subjects" below was 424, 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 350 participants (USA - 235 ; Canada -76 and; Germany - 39).

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	05 November 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	Canada: 93
Country: Number of subjects enrolled	United States: 279
Country: Number of subjects enrolled	Germany: 52
Worldwide total number of subjects	424
EEA total number of subjects	52

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)	393
From 65 to 84 years	30
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were screened and recruited at sites in US, Canada and Germany. 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:

424 met the inclusion/exclusion criteria and were randomized.

Period 1

Period 1 title	First treatment
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:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

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:

The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + Placebo in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo in 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:

The volume was 0.1 ml per injection.

Placebo - 0 U per 0.1 ml.

MT10109L - 4 U per 0.1 ml

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:

The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + MT10109L in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L 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:

The volume was 0.1 ml per injection.

MT10109L - 4 U per 0.1 ml

Number of subjects in period 1	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Started	86	171	167
Completed	76	153	157
Not completed	10	18	10
Consent withdrawn by subject	5	7	4
Physician decision	1	3	-
Adverse event, non-fatal	-	1	1
Pregnancy	-	1	-
Early termination, COVID-19	1	4	2
Lost to follow-up	3	2	3

Period 2

Period 2 title	Re-treatment 1
Is this the baseline period?	No
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:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

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:

The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + Placebo in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo the GL area.

Arm type	Experimental
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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:

The volume was 0.1 ml per injection.

Placebo - 0 U per 0.1 ml.

MT10109L - 4 U per 0.1 ml

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:

The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + MT10109L in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L 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:

The volume was 0.1 ml per injection.

MT10109L - 4 U per 0.1 ml

Number of subjects in period 2^[1]	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Started	75	150	155
Completed	69	141	150
Not completed	6	9	5
Consent withdrawn by subject	4	5	2
Physician decision	1	-	1
COVID-19	1	1	1
Lost to follow-up	-	3	1

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 period 1 (first treatment), who met the protocol-defined re-treatment criteria, were eligible to enter period 2 (re-treatment 1)

Period 3

Period 3 title	Re-treatment 2
Is this the baseline period?	No
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:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

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

Dosage and administration details:

The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + Placebo in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo 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: The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml. MT10109L - 4 U per 0.1 ml	
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:
The volume was 0.1 ml per injection. Placebo - 0 U per 0.1 ml.

Arm title	MT10109L in LCL + MT10109L in GL
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Arm description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L 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:
The volume was 0.1 ml per injection.
MT10109L - 4 U per 0.1 ml

Number of subjects in period 3^[2]	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Started	53	108	108
Completed	51	102	106
Not completed	2	6	2
Consent withdrawn by subject	2	1	2
Adverse event, non-fatal	-	2	-
COVID-19	-	2	-
Pregnancy	-	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 period 2 (re-treatment 1), who met the protocol-defined re-treatment criteria, were eligible to enter period 3 (re-treatment 2)

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

Reporting group title	MT10109L in LCL + Placebo in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo the GL area.

Reporting group title	MT10109L in LCL + MT10109L in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L the GL area.

Reporting group values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Number of subjects	86	171	167
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)	80	156	157
From 65-84 years	5	15	10
85 years and over	1	0	0
Age continuous Units: years			
arithmetic mean	48.6	47.7	49.1
standard deviation	± 12.32	± 11.56	± 10.37

Gender categorical Units: Subjects			
Female	71	143	141
Male	15	28	26

Reporting group values	Total		
Number of subjects	424		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	393		
From 65-84 years	30		
85 years and over	1		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	355		
Male	69		

Subject analysis sets

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

Subject analysis set description:

424 participants were included in the Intent-To-Treat (ITT) population (86 participants in the placebo group; 171 participants in the MT10109L in LCL + Placebo in GL; and 167 participants in the MT10109L in LCL + MT10109L in GL group).

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

Subject analysis set description:

350 participants were included in the modified Intent-To-Treat (ITT) population (70 participants in the placebo group; 138 participants in the MT10109L in LCL + Placebo in GL; and 142 participants in the MT10109L in LCL + MT10109L in GL group).

Reporting group values	Demographic and other Baseline Characteristics - ITT	Demographic and other Baseline Characteristics - mITT	
Number of subjects	424	350	
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)	393	324	
From 65-84 years	30	25	
85 years and over	1	1	
Age continuous			
Units: years			
arithmetic mean	48.5	48.8	
standard deviation	± 11.26	± 11.07	
Gender categorical			
Units: Subjects			
Female	355	297	
Male	69	53	

End points

End points reporting groups

Reporting group title	Placebo
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

Reporting group title	MT10109L in LCL + Placebo in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo the GL area.

Reporting group title	MT10109L in LCL + MT10109L in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L the GL area.

Reporting group title	Placebo
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

Reporting group title	MT10109L in LCL + Placebo in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo the GL area.

Reporting group title	MT10109L in LCL + MT10109L in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or

- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L the GL area.

Reporting group title	Placebo
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving the placebo in both LCL and GL areas.

Reporting group title	MT10109L in LCL + Placebo in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and placebo the GL area.

Reporting group title	MT10109L in LCL + MT10109L in GL
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Reporting group description:

The overall participants were randomized 2:2:1 to the following arms to receive:

- Placebo in both LCL and GL areas, or
- MT10109L 24 U (24 U in LCL area, placebo in GL area), or
- MT10109L 44 U (24 U in LCL area and 20 U in GL area),

This arm describes the data for participants receiving MT10109L in the LCL area and MT10109L the GL area.

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

424 participants were included in the Intent-To-Treat (ITT) population (86 participants in the placebo group; 171 participants in the MT10109L in LCL + Placebo in GL; and 167 participants in the MT10109L in LCL + MT10109L in GL group).

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

350 participants were included in the modified Intent-To-Treat (ITT) population (70 participants in the placebo group; 138 participants in the MT10109L in LCL + Placebo in GL; and 142 participants in the MT10109L in LCL + MT10109L in GL group).

Primary: Co-primary Efficacy endpoint: The % 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 Efficacy endpoint: The % 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
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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 Investigator 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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	70	138	142	
Units: Participants	3	78	86	

Statistical analyses

Statistical analysis title	MT10109L in LCL vs Placebo
Comparison groups	MT10109L in LCL + Placebo in GL v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[1]
Method	Cochran-Mantel-Haenszel

Notes:

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

Statistical analysis title	MT10109L in LCL plus MT10109L in GL vs Placebo
Comparison groups	MT10109L in LCL + MT10109L in GL v Placebo
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[2]
Method	Cochran-Mantel-Haenszel

Notes:

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

Primary: Primary Efficacy endpoint: The % 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 Efficacy endpoint: The % 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
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	70	138	142	
Units: Participants	2	60	67	

Statistical analyses

Statistical analysis title	MT10109L in LCL vs Placebo
Comparison groups	Placebo v MT10109L in LCL + Placebo in GL
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[3]
Method	Cochran-Mantel-Haenszel

Notes:

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

Statistical analysis title	MT10109L in LCL plus MT10109L in GL vs Placebo
Comparison groups	Placebo v MT10109L in LCL + MT10109L in GL
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[4]
Method	Cochran-Mantel-Haenszel

Notes:

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

Secondary: Sec Eff Endpoint 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 According to Inv Assmt

End point title	Sec Eff Endpoint 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 According to Inv Assmt
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	75	86	
Units: Days				
median (inter-quartile range (Q1-Q3))	119 (57.0 to 186.0)	94.0 (84.0 to 131.0)	93.0 (85.0 to 127.0)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Sec Eff Endpoint 2: The % of participants reporting mostly satisfied/very satisfied on a 5-point scale of very dissatisfied to very satisfied at Day 60 on the FLSQ follow-up version Item 5 for LCL
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	126	134	
Units: Participants	6	73	103	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 3: The % of participants with ≥ 20 -point improvement from baseline at Day 30 on the FLSQ Impact domain for LCL

End point title	Sec Eff Endpoint 3: The % of participants with ≥ 20 -point improvement from baseline at Day 30 on the FLSQ Impact domain for LCL
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	130	141	
Units: Participants	12	59	77	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 4: The % 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 ≥ 1 -grade improvement from baseline

End point title	Sec Eff Endpoint 4: The % 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 ≥ 1 -grade
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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.

End point type	Secondary
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End point timeframe:

Day 30

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	126	135	
Units: Participants	12	82	91	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 5: The % 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 is defined as achieving ≥ 1 -grade improvement from baseline

End point title	Sec Eff Endpoint 5: The % 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 is defined as achieving ≥ 1 -grade improvement from baseline
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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 participant FWS rating is presented here.

End point type	Secondary
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End point timeframe:

Day 30

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	125	136	
Units: Participants	6	73	84	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 6: The % of participants with a ≥ 20 -point improvement from baseline at Day 30 on the FLO-11© questionnaire total score for LCL

End point title	Sec Eff Endpoint 6: The % of participants with a ≥ 20 -point improvement from baseline at Day 30 on the FLO-11© questionnaire total score for LCL
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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 FLO-11 questionnaire for LCL (eg, reported less emotional and appearance-related impacts of upper-facial lines) is presented here.

End point type	Secondary
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End point timeframe:

Day 30

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	131	141	
Units: Participants	11	74	98	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 7: The % of participants with a > 4 -point improvement from baseline at Day 30 on the FLO-11 questionnaire Item 2 for LCL

End point title	Sec Eff Endpoint 7: The % of participants with a > 4 -point improvement from baseline at Day 30 on the FLO-11 questionnaire Item 2 for LCL
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	131	140	
Units: Participants	9	60	86	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Eff Endpoint 8: The % of participants with a > 4-point improvement from baseline at Day 30 on the FLO-11 questionnaire Item 5 for LCL

End point title	Sec Eff Endpoint 8: The % of participants with a > 4-point improvement from baseline at Day 30 on the FLO-11 questionnaire Item 5 for LCL
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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 in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	131	138	
Units: Participants	6	58	71	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 1a: Mean Change From Baseline in Systolic Blood Pressure (BP)

End point title	Sec Safety Endpoint 1a: Mean Change From Baseline in Systolic Blood Pressure (BP)
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	149	157	
Units: mmHg				
arithmetic mean (standard deviation)	1.0 (± 11.6)	-0.4 (± 12.29)	-0.3 (± 13.67)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 1b: Mean Change From Baseline in Diastolic Blood Pressure (BP)

End point title	Sec Safety Endpoint 1b: Mean Change From Baseline in Diastolic Blood Pressure (BP)
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

From Baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	149	157	
Units: mmHg				
arithmetic mean (standard deviation)	-1.2 (± 8.61)	-1.4 (± 8.34)	-0.7 (± 9.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 2: Mean Change From Baseline in Pulse Rate

End point title	Sec Safety Endpoint 2: Mean Change From Baseline in Pulse Rate
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit at study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	149	157	
Units: beats/min				
arithmetic mean (standard deviation)	-0.7 (± 11.2)	0.9 (± 10.54)	-0.4 (± 11.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 3: Mean Change From Baseline in Respiratory Rate

End point title	Sec Safety Endpoint 3: Mean Change From Baseline in Respiratory Rate
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit at study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	149	157	
Units: breaths/min				
arithmetic mean (standard deviation)	-0.4 (± 2.03)	-0.3 (± 2.04)	-0.6 (± 2.47)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 4: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - Mean Heart Rate

End point title	Sec Safety Endpoint 4: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - Mean Heart Rate
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit at day study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: beats/min				
arithmetic mean (standard deviation)	3.3 (± 10.34)	4.2 (± 9.35)	2.7 (± 8.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 5: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - PR Interval

End point title	Sec Safety Endpoint 5: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - PR Interval
End point description: Change from baseline at study exit.	
All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.	
End point type	Secondary
End point timeframe: Change from baseline to study exit	

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	-0.5 (± 9.36)	-0.7 (± 12.37)	0.0 (± 11.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 6: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QRS Duration

End point title	Sec Safety Endpoint 6: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QRS Duration
End point description: Change from baseline at study exit.	
All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.	
End point type	Secondary
End point timeframe: Change from baseline to study exit	

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	0.0 (± 6.16)	0.4 (± 5.35)	1.6 (± 8.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 7: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QT Interval

End point title	Sec Safety Endpoint 7: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QT Interval
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	-8.6 (± 25.07)	-10.4 (± 21.96)	-9.2 (± 21.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 8: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcB Interval

End point title	Sec Safety Endpoint 8: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcB Interval
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	0.9 (\pm 17.34)	1.6 (\pm 16.64)	-1.5 (\pm 16.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 9: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcF Interval

End point title	Sec Safety Endpoint 9: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcF Interval
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	-2.4 (\pm 14.21)	-2.7 (\pm 13.57)	-4.2 (\pm 13.65)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 10: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - RR Interval

End point title	Sec Safety Endpoint 10: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - RR Interval
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End point description:

Change from baseline at study exit.

All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection.

End point type	Secondary
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End point timeframe:

Change from baseline to study exit

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	149	157	
Units: milliseconds				
arithmetic mean (standard deviation)	-42.6 (± 137.27)	-53.0 (± 120.85)	-35.0 (± 114.66)	

Statistical analyses

No statistical analyses for this end point

Secondary: Sec Safety Endpoint 11: Number of Participants With Binding and Neutralizing Antibodies

End point title	Sec Safety Endpoint 11: Number of Participants With Binding and Neutralizing Antibodies
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End point description:

Only samples that tested positive in the binding antibody confirmatory assay were evaluated for neutralizing antibodies. The participants with positive neutralizing antibodies are only shown.

End point type	Secondary
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End point timeframe:

On Day 360

End point values	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	145	150	
Units: Participants	0	0	0	

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-Emergent Adverse Events (TEAEs) that started or worsened after the first dose of study intervention and within 30 days after the last visit or study exit (Day 360 unless the participant exits earlier) that started or worsened after the first dose

Adverse event reporting additional description:

Treatment-Emergent Adverse Events (TEAEs)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo in both Lateral Canthal Lines (LCL) and Glabellar Lines (GL) areas

Reporting group title	MT10109L in LCL + Placebo in GL
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Reporting group description:

MT10109L was injected into the LCL and Placebo into the GL

Reporting group title	MT10109L in LCL + MT10109L in GL
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Reporting group description:

MT10109L was injected into the LCL and MT10109L into the GL

Serious adverse events	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 86 (4.65%)	11 / 171 (6.43%)	5 / 168 (2.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 86 (1.16%)	3 / 171 (1.75%)	2 / 168 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 86 (0.00%)	0 / 171 (0.00%)	1 / 168 (0.60%)
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			

subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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 [F]			
subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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
Immune system disorders			
Allergy to arthropod sting			

subjects affected / exposed	0 / 86 (0.00%)	0 / 171 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 86 (1.16%)	1 / 171 (0.58%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis microscopic			
subjects affected / exposed	1 / 86 (1.16%)	0 / 171 (0.00%)	0 / 168 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 86 (1.16%)	0 / 171 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 86 (0.00%)	0 / 171 (0.00%)	1 / 168 (0.60%)
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 / 86 (0.00%)	2 / 171 (1.17%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	0 / 86 (0.00%)	1 / 171 (0.58%)	0 / 168 (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

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

Non-serious adverse events	Placebo	MT10109L in LCL + Placebo in GL	MT10109L in LCL + MT10109L in GL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 86 (39.53%)	60 / 171 (35.09%)	74 / 168 (44.05%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 86 (3.49%)	9 / 171 (5.26%)	22 / 168 (13.10%)
occurrences (all)	3	9	22
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	8 / 86 (9.30%)	15 / 171 (8.77%)	15 / 168 (8.93%)
occurrences (all)	8	15	15
Injection site bruising			
subjects affected / exposed	6 / 86 (6.98%)	7 / 171 (4.09%)	6 / 168 (3.57%)
occurrences (all)	6	7	6
Gastrointestinal disorders			
Injection site haemorrhage			
subjects affected / exposed	6 / 86 (6.98%)	9 / 171 (5.26%)	6 / 168 (3.57%)
occurrences (all)	6	9	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 86 (6.98%)	16 / 171 (9.36%)	15 / 168 (8.93%)
occurrences (all)	6	16	15
Upper respiratory tract infection			
subjects affected / exposed	5 / 86 (5.81%)	4 / 171 (2.34%)	10 / 168 (5.95%)
occurrences (all)	5	4	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2019	<p>Substantial, made to integrate feedback and recommendations from health authorities and improve clarity of study processes:</p> <ul style="list-style-type: none">• Clarified the primary objective and endpoint, added secondary objectives and efficacy and safety endpoints.• Added vital sign measurements, ECG assessments, and collection of blood samples for hematology and chemistry testing for Days 30 and 120. Vital sign measurements were added for 30 days after each retreatment; ECG assessments were added for the days of Retreatments 1 and 2 and 30 days after each retreatment.• Added text to clarify that collection of AEs at follow-up visits only applied to participants who received study intervention, added a new section related to which type of AESI were selected for this study, revised the timeframe for which to report nonserious AESIs, revised the duration after which an AE would not be counted as a TEAE, and added a paragraph describing analysis of TEAEs related to PDSOT and monitoring of PDSOT.• Revised the description of which pregnancy outcomes were considered SAEs.• Added statement in primary analyses describing the condition under which MT10109L 44 U was to be tested, added text describing imputation methods, replaced site with baseline LCL severity at maximum smile as assessed by the clinician (investigator or subinvestigator) as stratification factors, added text to describe the methods of sensitivity analyses, provided details on the ranking order for hierarchical testing of MT10109L 24 U and MT10109L 44 U versus placebo for secondary analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported