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 Glabellar Lines.

Summary

EudraCT number	2018-004384-31
Trial protocol	BE
Global end of trial date	25 January 2021

Results information

Result version number	v1 (current)
This version publication date	13 December 2023
First version publication date	13 December 2023

Trial information

Trial identification

Sponsor protocol code	MT10109L-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03795922
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 2-69015424,
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	13 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 MT10109L and placebo for the treatment of GL in participants with moderate to severe GL.

The total global enrollment (as presented in the "Population of Trial Subjects" below was 234, 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 191 participants (USA - 153; Russia - 21 and; Belgium - 17).

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	24 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	Belgium: 26
Country: Number of subjects enrolled	United States: 178
Country: Number of subjects enrolled	Russian Federation: 30
Worldwide total number of subjects	234
EEA total number of subjects	26

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)	218
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were screened and recruited at sites in US, Belgium 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:

234 met the inclusion/exclusion criteria and were randomized.

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 Glabellar Lines (GL): 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:

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

Arm title	MT10109L

Arm description:

MT10109L was injected into the Glabellar Lines (GL): initial double-blind treatment on Day 1

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:

5 injection sites. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 20 U

Number of subjects in period 1	Placebo	MT10109L
Started	80	154
Completed	71	138
Not completed	9	16
Consent withdrawn by subject	4	10
Early termination, COVID, Family issue	1	2
Adverse event, non-fatal	2	1
Pregnancy	-	1
Lost to follow-up	2	2

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 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:

2 treatment cycles in the open-label period. 5 injection sites per treatment. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 20 U per treatment cycle

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

Arm description:

Participants from the experimental arm of Period 1, who met protocol-defined re-treatment criteria, were eligible to receive up to two additional 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. 5 injection sites per treatment. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 20 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	69	136
Completed	65	129
Not completed	4	7
Consent withdrawn by subject	1	2
Physician decision	1	2
Early termination, COVID, Family issue	2	2
Lost to follow-up	-	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: 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. 5 injection sites per treatment. 0.1 ml per injection. Placebo - 4 U per 0.1 ml. Total = 20 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 re-treatment criteria, were eligible to receive up to two 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. 5 injection sites per treatment. 0.1 ml per injection. MT10109L - 4 U per 0.1 ml. Total = 20 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	52	99
Completed	52	97
Not completed	0	2
Consent withdrawn by subject	-	1
Protocol deviation	-	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: 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 Glabellar Lines (GL): initial double-blind treatment on Day 1.	
Reporting group title	MT10109L
Reporting group description:	
MT10109L was injected into the Glabellar Lines (GL): initial double-blind treatment on Day 1	

Reporting group values	Placebo	MT10109L	Total
Number of subjects	80	154	234
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)	77	141	218
From 65-84 years	3	13	16
85 years and over	0	0	0
Adults (18 - 64)	0	0	0
Age continuous Units: years			
arithmetic mean	46.4	47.3	
standard deviation	± 11.57	± 12.64	-
Gender categorical Units: Subjects			
Female	76	140	216
Male	4	14	18

Subject analysis sets	
Subject analysis set title	Demographic and other Baseline Characteristics - ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
234 participants were included in the Intent To Treat (ITT) population (80 participants in the placebo group and 154 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:	
191 participants were included in the modified Intent To Treat (mITT) population (68 participants in the placebo group and 123 participants in the MT10109L group).	

Reporting group values	Demographic and other Baseline Characteristics - ITT	Demographic and other Baseline Characteristics - mITT	
Number of subjects	234	191	
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)	218	179	
From 65-84 years	16	12	
85 years and over	0	0	
Adults (18 - 64)	0	0	
Age continuous Units: years			
arithmetic mean	47.0	48.3	
standard deviation	± 12.27	± 11.49	
Gender categorical Units: Subjects			
Female	216	178	
Male	18	13	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo was injected into the Glabellar Lines (GL): initial double-blind treatment on Day 1.	
Reporting group title	MT10109L
Reporting group description:	
MT10109L was injected into the Glabellar Lines (GL): 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 in the placebo arm, who met retreatment criteria, were allowed up to 2 MT10109L treatments.	
Reporting group title	MT10109L re-treatment 1 for experimental arm in cycle 1
Reporting group description:	
Participants from the experimental arm of Period 1, who met protocol-defined re-treatment criteria, were eligible to receive up to two additional MT10109L 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 re-treatment criteria, were eligible to receive up to two 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:	
234 participants were included in the Intent To Treat (ITT) population (80 participants in the placebo group and 154 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:	
191 participants were included in the modified Intent To Treat (mITT) population (68 participants in the placebo group and 123 participants in the MT10109L group).	

Primary: Co-Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Participant Assessment of GL Severity at Maximum Frown 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 Participant Assessment of GL Severity at Maximum Frown 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 GL severity at maximum frown 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	68	123		
Units: Participants	3	80		

Statistical analyses

Statistical analysis title	% of Participants Achieving Co-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	191
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 GL baseline severity.

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

End point title	Primary: The Percentage of Participants Achieving None or Mild on the FWS According to Investigator Assessment of GL Severity at Maximum Frown 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 GL severity at maximum frown 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		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	123		
Units: Participants	3	95		

Statistical analyses

Statistical analysis title	% of Participants Achieving Primary Endpoint

Statistical analysis description:

Primary efficacy analyses endpoints were carried out using the modified Intent-To-Treat (mITT) analysis set, which 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	191
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 GL baseline severity.

Secondary: Secondary 4: The Percentage of Responders for Investigator Assessments of GL 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 ≥1-grade Improvement from Baseline

End point title	Secondary 4: The Percentage of Responders for Investigator Assessments of GL 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 ≥1-grade Improvement from Baseline

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 GL 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	62	115		
Units: Participants	23	76		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 1:The Duration of GL Treatment Effect, Estimated as the Median Time to Return to Moderate or Severe GL at Maximum Frown, in Participants Who Achieved a Rating of None or Mild from Baseline in GL Severity at Maximum Frown at Day 30

End point title	Secondary 1:The Duration of GL Treatment Effect, Estimated as the Median Time to Return to Moderate or Severe GL at Maximum Frown, in Participants Who Achieved a Rating of None or Mild from Baseline in GL Severity at Maximum Frown 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 GL 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 GL severity at maximum frown 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 1 (first treatment) to Day 180

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	95		
Units: Days				
median (inter-quartile range (Q1-Q3))	64 (59 to 126)	120 (87 to 149)		

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 at Day 60 on the FLSQ Follow-up Version Item 5 for GL

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 at Day 60 on the FLSQ Follow-up Version Item 5 for GL

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	63	120		
Units: Participants	5	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 3: The Percentage of Participants with ≥20-point Improvement from Baseline at Day 30 on the FLSQ Impact Domain for GL

End point title	Secondary 3: The Percentage of Participants with ≥20-point Improvement from Baseline at Day 30 on the FLSQ Impact Domain for GL

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	66	121		
Units: Participants	6	90		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 5: The Percentage of Responders for Participant Assessments of GL 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 ≥1-grade Improvement at Day 30

End point title	Secondary 5: The Percentage of Responders for Participant Assessments of GL 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 ≥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 GL severity at rest based on participant 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	62	115		
Units: Participants	7	76		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 6: The Percentage of participants with a ≥ 20-point improvement from baseline at Day 30 on the FLO-11© questionnaire total score for GL

End point title	Secondary 6: The Percentage of participants with a ≥ 20-point improvement from baseline at Day 30 on the FLO-11© questionnaire total score for GL

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 GL (eg, reported less emotional and appearance-related impacts of upper-facial lines) 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	66	123		
Units: Participants	4	92		

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 2 for GL

End point title	Secondary 7: The Percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 2 for GL

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 GL (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	66	123		
Units: Participants	4	77		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 8: The Percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 5 for GL

End point title	Secondary 8: The Percentage of participants with a > 4-point improvement from baseline at Day 30 on FLO-11 questionnaire Item 5 for GL

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 GL (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	66	119		
Units: Participants	6	65		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 9: Mean Change From Baseline in Vital Signs - Systolic Blood Pressure (BP)

End point title	Secondary 9: Mean Change From Baseline in Vital Signs - Systolic Blood Pressure (BP)

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
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or Early exit.

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	133		
Units: mm Hg				
arithmetic mean (standard deviation)	0.3 (± 13.26)	-0.6 (± 15.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 10: Mean Change From Baseline in Vital Signs - Diastolic Blood Pressure (BP)

End point title	Secondary 10: Mean Change From Baseline in Vital Signs - Diastolic Blood Pressure (BP)

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.
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	133		
Units: mm Hg				
arithmetic mean (standard deviation)	0.5 (± 10.04)	-1.9 (± 10.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 11: Mean Change From Baseline in Vital Signs - Respiratory rate

End point title	Secondary 11: Mean Change From Baseline in Vital Signs - Respiratory rate

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
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	133		
Units: breath/min				
arithmetic mean (standard deviation)	-0.3 (± 2.44)	-0.3 (± 2.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 12: Mean Change From Baseline in Vital Signs - Pulse Rate

End point title	Secondary 12: Mean Change From Baseline in Vital Signs - Pulse Rate

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
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	133		
Units: beats/min				
arithmetic mean (standard deviation)	2.5 (± 10.35)	0.4 (± 10.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 13: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - Heart Rate

End point title	Secondary 13: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - Heart Rate

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.
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: beats/min				
arithmetic mean (standard deviation)	4.8 (± 10.38)	2.8 (± 8.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 14: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - PR Interval

End point title	Secondary 14: 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
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	-1.2 (± 11.67)	-1.2 (± 11.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 15: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QRS Duration

End point title	Secondary 15: 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
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	0.4 (± 6.65)	1.2 (± 6.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 16: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QT Interval

End point title	Secondary 16: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QT 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

In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	-11.7 (± 23.87)	-8.4 (± 19.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 17: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcB Interval

End point title	Secondary 17: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcB 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.

In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	2.7 (± 18.69)	0.0 (± 17.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 18: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcF Interval

End point title	Secondary 18: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - QTcF 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.
In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	-2.4 (± 15.43)	-2.9 (± 14.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 19: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - RR Interval

End point title	Secondary 19: Mean Change From Baseline in Electrocardiogram (ECG) Parameters - RR 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.

In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments.

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	130		
Units: milliseconds				
arithmetic mean (standard deviation)	-64.6 (± 127.1)	-39.3 (± 106.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary 20:Number of Participants With Binding and Neutralizing Antibodies

End point title	Secondary 20:Number of Participants With Binding and Neutralizing Antibodies

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.
All safety analyses were carried out using Safety Population which includes all subjects who received at least 1 study treatment injection. In open-label period, subjects from both placebo group and MT10109L group who met re-treatment criteria were allowed up to two MT10109L re-treatments

End point type	Secondary

End point timeframe:

Day 360 or early exit

End point values	Placebo	MT10109L		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	154		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

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:

Safety analyses were carried out using the Safety population (participants who received at least 1 dose of study intervention). Placebo participants who entered open-label phase (post Day 180) and received study intervention are counted in MT10109L Group. Thus, overall number of participants in MT10109L Group is greater than the participant flow.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

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

Reporting group title	MT10109L

Reporting group description:

MT10109L was injected into the Glabellar Lines (GL): 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.

Serious adverse events	Placebo	MT10109L	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 80 (3.75%)	5 / 223 (2.24%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer Stage II			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma in situ			

subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 80 (1.25%)	0 / 223 (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	1 / 80 (1.25%)	0 / 223 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional Overdose			
subjects affected / exposed	1 / 80 (1.25%)	0 / 223 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectal prolapse			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 223 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 223 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
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	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 80 (10.00%)	32 / 223 (14.35%)	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 80 (5.00%)	22 / 223 (9.87%)	
occurrences (all)	4	22	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	4 / 80 (5.00%)	16 / 223 (7.17%)	
occurrences (all)	4	16	

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