



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | MT10109L-002 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03785145 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | IND: 121473 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Medytox Inc |
| Sponsor organisation address | 78, Gangni 1-gil, Ochang-eup, Cheongwon-gu, Cheongju-si, Korea, Republic of, 28126 |
| Public contact | Young Ryu, Medytox Inc., 82 2-6901-5424, |
| Scientific contact | Gyungjin Heo, Medytox Inc., 82 2-6901-5839, gjheo@medytox.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 September 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 February 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 January 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

The study was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonisation (ICH)/Good Clinical Practice (GCP) and other Guidelines, and applicable laws and regulations.

An ICF approved by each study center's IEC/IRB was signed by the participant or their legally authorized representative and the authorized person obtaining the ICF before the participant was entered in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 December 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

| | |
|----------|---|
| In utero | 0 |
|----------|---|

| | |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 224 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Blinding implementation details:

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|----------|
| Arm title | MT10109L |
|------------------|----------|

Arm description:

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

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

Dosage and administration details:

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

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

Period 2

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

Arms

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants from the previous treatment period who met a protocol-defined re-treatment criteria entered into the next treatment period.

Period 3

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

Arms

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

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|--|
| Arm title | MT10109L re-treatment 2 for experimental arm |
|------------------|--|

Arm description:

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

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

Dosage and administration details:

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

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

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants from the previous treatment period who met a protocol-defined re-treatment criteria entered into the next treatment period.

Baseline characteristics

Reporting groups

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

| Reporting group values | Placebo | MT10109L | Total |
|---|---------|----------|-------|
| Number of subjects | 77 | 158 | 235 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 75 | 149 | 224 |
| From 65-84 years | 2 | 9 | 11 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 46.1 | 46.6 | |
| standard deviation | ± 11.09 | ± 11.43 | - |
| Gender categorical Units: Subjects | | | |
| Female | 61 | 127 | 188 |
| Male | 16 | 31 | 47 |

Subject analysis sets

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

| Reporting group values | Demographic and other Baseline Characteristics - ITT | Demographic and other Baseline Characteristics - mITT | |
|--|--|---|--|
| Number of subjects | 235 | 181 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 224 | 172 | |
| From 65-84 years | 11 | 9 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 46.4 | 48.0 | |
| standard deviation | ± 11.30 | ± 10.8 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 188 | 152 | |
| Male | 47 | 29 | |

End points

End points reporting groups

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

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

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

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

Statistical analyses

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

Statistical analysis description:

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

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

Notes:

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

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

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

End point description:

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

The data here presents the percentage of participants who had LCL severity at maximum smile of none or mild based on participant FWS rating at Cycle 1 Day 30.

FWS is 4-point grading scale, where 0=none, 1=mild, 2=moderate, and 3=severe.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 30

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

Statistical analyses

| Statistical analysis title | % of Participants achieving primary endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

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

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

Notes:

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

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

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

End point description:

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

The investigator evaluates the participant's LCL severity using a 4-grade FWS scale (0 to 3) where 0=none and 3 = severe. The outcome is measured as median time to loss of treatment effect (i.e., return to moderate or severe LCL severity at maximum smile using the FWS).

FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 30

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 60 | |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The percentage of participants who achieved a ≥ 1 -grade improvement from baseline LCL severity at rest based on investigator FWS rating is presented here.

FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 30 | |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The percentage of participants who achieved a ≥ 1 -grade improvement from baseline LCL severity at rest based on participants FWS rating is presented here.

FWS is a 4-grade scale (0 to 3) where 0 = none and 3 = severe.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 30 | |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The percentage of participants who achieved a ≥ 20 -point improvement from baseline on the FLSQ impact domain (eg, reported a good improvement of the facial lines negative impact) are presented here.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 30

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The percentage of participants who achieved a ≥ 4 -point improvement from baseline on the FLO-11 questionnaire item 2 for LCL (eg, reported good improvement in the appearance of skin age) is presented here.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 30

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The percentage of participants who achieved a ≥ 4 -point improvement from baseline on the FLO-11 questionnaire item 5 for LCL (eg, reported good improvement in attractiveness) is presented here.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 30

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | MT10109L |
|-----------------------|----------|

Reporting group description:

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

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Non-serious adverse events recorded were below the threshold of 5%.

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported