



## Clinical trial results:

### A Phase 3, Multi-center, Open-label, Safety Study of Oral Edaravone Administered over 48 Weeks in Subjects with Amyotrophic Lateral Sclerosis (ALS)

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2019-002108-41  |
| Trial protocol           | DE IT           |
| Global end of trial date | 07 October 2021 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1             |
| This version publication date  | 26 August 2023 |
| First version publication date | 26 August 2023 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | MT-1186-A01 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |  |
|------------------------------------|--|
| ISRCTN number                      | -  |
| ClinicalTrials.gov id (NCT number) | NCT04165824  |
| WHO universal trial number (UTN)   | -  |
| Other trial identifiers            | Japan Registry of Clinical Trials (jRCT): jRCT2080224982 |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Mitsubishi Tanabe Pharma America, Inc.  |
| Sponsor organisation address | 525 Washington Blvd, Suite 1100, Jersey City, United States, 07310                    |
| Public contact               | General Information, Mitsubishi Tanabe Pharma Europe Ltd, regulatory@mt-pharma-eu.com |
| Scientific contact           | General Information, Mitsubishi Tanabe Pharma Europe Ltd, regulatory@mt-pharma-eu.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                       | 24 November 2021 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 07 October 2021  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 07 October 2021  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of Oral Edaravone in subjects with ALS over 24 and 48 weeks.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice as required by the International Conference on Harmonization guidelines, applicable regional and local legislation, and standard operating procedures in place at Mitsubishi Tanabe Pharma America Inc and at the contracted vendor. All participants underwent screening aimed at minimizing the likelihood and impact of potential risks of MT-1186. In addition, regular safety monitoring during the study period for all participants ensured that any unanticipated effects of study participation were identified promptly and managed appropriately.

Risk minimization measures were also employed during the study as per the risk-benefit assessment for potential anticipated risks.

A participant was to be withdrawn from the study if ANY of the protocol specific withdrawal criteria were met including voluntary wish of participant to withdraw from further participation

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 13 November 2019 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Italy: 9          |
| Country: Number of subjects enrolled | Japan: 65         |
| Country: Number of subjects enrolled | United States: 71 |
| Country: Number of subjects enrolled | Canada: 23        |
| Country: Number of subjects enrolled | France: 11        |
| Country: Number of subjects enrolled | Germany: 6        |
| Worldwide total number of subjects   | 185               |
| 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)                      | 120 |
| From 65 to 84 years                       | 65  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment Started on 26 Nov 2019 and was completed on 29 Oct 2020, globally: USA, Canada, Germany, Italy, France, Japan  
Subjects Screened: 216  
Screen Failures: 31  
Subjects Enrolled in Study: 185  
Subjects who completed week 48: 139  
Subjects who discontinued during week 48: 46

### Pre-assignment

Screening details:

Subjects were screened globally following protocol specific inclusion and exclusion criteria  
Subjects Screened: 216  
Screen Failures: 31  
Reason for Screen Failure  
Study Entry Criteria Not Met (25)  
Withdrawal by Subjects (2)  
Covid 19 (4)

### Period 1

|                              |                              |
|------------------------------|------------------------------|
| Period 1 title               | MT-1186-A01 (overall period) |
| Is this the baseline period? | Yes                          |
| Allocation method            | Non-randomised - controlled  |
| Blinding used                | Not blinded                  |

### Arms

|  |                                |
|--|--------------------------------|
| Arm title                              | MT-1186                        |
| Arm description:                       |                                |
| MT-1186 105mg (2 weeks On/Off )        |                                |
| Arm type                               | Experimental                   |
| Investigational medicinal product name | MT-1186                        |
| Investigational medicinal product code |                                |
| Other name                             | Edaravone                      |
| Pharmaceutical forms                   | Suspension for oral suspension |
| Routes of administration               | Oral use                       |

Dosage and administration details:

MT-1186 oral suspension (21 mg/mL) in amber multi-use bottles, adapters, and oral syringes were provided for each subject, for the duration of their participation in the study. Suspension bottles contained approximately 735 mg of MT-1186 in 35 mL for the first cycle and approximately 1050 mg of MT-1186 in 50 mL for Cycles 2 through 12.

All subjects enrolled received the following dose regimen:

- \* An initial treatment cycle with daily dosing for 14 days, followed by a 14-day drug-free period.
- \* Subsequent treatment cycles with daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods. Treatment cycles were every 4 weeks.

The dose of MT-1186 was taken after an overnight fast and subjects continued to fast at least 1 to 2 hours postdose before the next meal (eg, breakfast)

| <b>Number of subjects in period 1</b> | MT-1186 |
|---------------------------------------|---------|
| Started                               | 185     |
| Completed                             | 139     |
| Not completed                         | 46      |
| Physician decision                    | 1       |
| Consent withdrawn by subject          | 17      |
| Adverse event, non-fatal              | 23      |
| Other                                 | 5       |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | MT-1186-A01 |
|-----------------------|-------------|

Reporting group description: -

| Reporting group values                             | MT-1186-A01 | Total |  |
|--|-------------|-------|--|
| Number of subjects                                 | 185         | 185   |  |
| 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)                               | 120         | 120   |  |
| From 65-84 years                                   | 65          | 65    |  |
| 85 years and over                                  | 0           | 0     |  |
| Gender categorical                                 |             |       |  |
| Units: Subjects                                    |             |       |  |
| Female   | 66          | 66    |  |
| Male   | 119         | 119   |  |
| Ethnicity (NIH/OMB)                                |             |       |  |
| Units: Subjects                                    |             |       |  |
| Hispanic or Latino                                 | 3           | 3     |  |
| Not Hispanic or Latino                             | 177         | 177   |  |
| Unknown or Not Reported                            | 5           | 5     |  |

### Subject analysis sets

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | Full Analysis |
|----------------------------|---------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Analysis Population:

Enrolled Population: The enrolled population set is all subjects who were found eligible and signed ICF to participate in the study.

Safety Analysis Population: The safety analysis population set is defined as all enrolled subjects who received at least 1 dose of oral edaravone

Pharmacokinetic (PK) Population: PK population includes all subjects who receive at least 1 dose of oral edaravone and who have at least 1 post-dose value for plasma concentration without important protocol deviations which may affect the PK of oral edaravone.

| Reporting group values | Full Analysis |  |  |
|------------------------|---------------|--|--|
| Number of subjects     | 185           |  |  |
| Age categorical        |               |  |  |
| Units: Subjects        |               |  |  |
| In utero               | 0             |  |  |

|   |     |  |  |
|---|-----|--|--|
| Preterm newborn infants<br>(gestational age < 37 wks) | 0   |  |  |
| Newborns (0-27 days)                                  | 0   |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0   |  |  |
| Children (2-11 years)                                 | 0   |  |  |
| Adolescents (12-17 years)                             | 0   |  |  |
| Adults (18-64 years)                                  | 120 |  |  |
| From 65-84 years                                      | 65  |  |  |
| 85 years and over                                     | 0   |  |  |
| Gender categorical<br>Units: Subjects                 |     |  |  |
| Female  | 66  |  |  |
| Male  | 119 |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects                |     |  |  |
| Hispanic or Latino                                    | 3   |  |  |
| Not Hispanic or Latino                                | 177 |  |  |
| Unknown or Not Reported                               | 5   |  |  |

## End points

### End points reporting groups

|  |               |
|--|---------------|
| Reporting group title  | MT-1186       |
| Reporting group description:<br>MT-1186 105mg (2 weeks On/Off )  |               |
| Subject analysis set title   | Full Analysis |
| Subject analysis set type  | Full analysis |
| Subject analysis set description:<br>Analysis Population:<br>Enrolled Population: The enrolled population set is all subjects who were found eligible and signed ICF to participate in the study.<br>Safety Analysis Population: The safety analysis population set is defined as all enrolled subjects who received at least 1 dose of oral edaravone<br>Pharmacokinetic (PK) Population: PK population includes all subjects who receive at least 1 dose of oral edaravone and who have at least 1 post-dose value for plasma concentration without important protocol deviations which may affect the PK of oral edaravone. |               |

### Primary: Number of Participants with Treatment Emergent Adverse Events

|                                  |  |
|----------------------------------|--|
| End point title                  | Number of Participants with Treatment Emergent Adverse Events <sup>[1]</sup> |
| End point description:           |  |
| End point type                   | Primary  |
| End point timeframe:<br>48 Weeks |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study is a long-term, open-label safety study. As a result, no formal hypothesis testing is planned for this study. The long-term safety and tolerability of oral edaravone was evaluated in exploratory manner using descriptive statistics. For exploratory efficacy analysis, point estimates and their associated 95% Confidence Interval was presented.

| End point values                                | MT-1186         | Full Analysis        |  |  |
|---|-----------------|----------------------|--|--|
| Subject group type                              | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed                     | 185             | 185                  |  |  |
| Units: Subjects                                 |                 |                      |  |  |
| Any TEAE  | 175             | 175                  |  |  |
| Any TEAE Related to Study Treatment             | 46              | 46                   |  |  |
| Any Severe TEAE                                 | 34              | 34                   |  |  |
| Any TESAE                                       | 48              | 48                   |  |  |
| TEAE Leading to Study Treatment Discontinuation | 16              | 16                   |  |  |
| Any TEAE Leading to Death                       | 12              | 12                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Treatment Emergent Adverse Events



|                        |  |
|------------------------|--|
| End point title        | Number of Treatment Emergent Adverse Events <sup>[2]</sup> |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   |  |
| 48 Weeks               |  |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This study is a long-term, open-label safety study. As a result, no formal hypothesis testing is planned for this study. The long-term safety and tolerability of oral edaravone was evaluated in exploratory manner using descriptive statistics. For exploratory efficacy analysis, point estimates and their associated 95% Confidence Interval was presented.

| End point values                                | MT-1186         | Full Analysis        |  |  |
|---|-----------------|----------------------|--|--|
| Subject group type                              | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed                     | 185             | 185                  |  |  |
| Units: Events                                   |                 |                      |  |  |
| Any TEAE  | 961             | 961                  |  |  |
| Any TEAE related to study treatment             | 79              | 79                   |  |  |
| Any severe TEAE                                 | 58              | 58                   |  |  |
| Any TESAЕ                                       | 62              | 62                   |  |  |
| TEAE leading to study treatment discontinuation | 22              | 22                   |  |  |
| Any TEAE leading to death                       | 13              | 13                   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Time to Death, Tracheostomy or Permanent Assisted Mechanical Ventilation

|                        |  |
|------------------------|--|
| End point title        | Time to Death, Tracheostomy or Permanent Assisted Mechanical Ventilation |
| End point description: |  |
| End point type         | Other pre-specified  |
| End point timeframe:   |  |
| 48 Weeks               |  |

| End point values                          | MT-1186         | Full Analysis        |  |  |
|---|-----------------|----------------------|--|--|
| Subject group type                        | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed               | 185             | 185                  |  |  |
| Units: Events                             |                 |                      |  |  |
| Death                                     | 14              | 14                   |  |  |
| Tracheostomy                              | 0               | 0                    |  |  |
| Permanent Assisted Mechanical Ventilation | 5               | 5                    |  |  |

|          |     |     |  |  |
|----------|-----|-----|--|--|
| Censored | 166 | 166 |  |  |
|----------|-----|-----|--|--|

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

48 weeks

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | MT-1186 |
|-----------------------|---------|

Reporting group description:

MT-1186 105mg (2 weeks On/Off )

| Serious adverse events                            | MT-1186           |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events |                   |  |  |
| subjects affected / exposed                       | 48 / 185 (25.95%) |  |  |
| number of deaths (all causes)                     | 14                |  |  |
| number of deaths resulting from adverse events    | 12                |  |  |
| Investigations                                    |                   |  |  |
| Oxygen saturation decreased                       |                   |  |  |
| subjects affected / exposed                       | 1 / 185 (0.54%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |
| Weight decreased                                  |                   |  |  |
| subjects affected / exposed                       | 2 / 185 (1.08%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 2             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |
| Injury, poisoning and procedural complications    |                   |  |  |
| Fall  |                   |  |  |
| subjects affected / exposed                       | 2 / 185 (1.08%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 2             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |
| Patella fracture                                  |                   |  |  |
| subjects affected / exposed                       | 1 / 185 (0.54%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |

|  |                  |  |  |
|--|------------------|--|--|
| Lower limb fracture                                  |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Cardiac disorders                                    |                  |  |  |
| Atrial fibrillation                                  |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Supraventricular tachycardia                         |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Surgical and medical procedures                      |                  |  |  |
| Gastrostomy  |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Nervous system disorders                             |                  |  |  |
| Amyotrophic lateral sclerosis                        |                  |  |  |
| subjects affected / exposed                          | 12 / 185 (6.49%) |  |  |
| occurrences causally related to treatment / all      | 0 / 12           |  |  |
| deaths causally related to treatment / all           | 0 / 2            |  |  |
| Muscle spasticity                                    |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| General disorders and administration site conditions |                  |  |  |
| Gait disturbance                                     |                  |  |  |
| subjects affected / exposed                          | 1 / 185 (0.54%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 1            |  |  |
| deaths causally related to treatment / all           | 0 / 0            |  |  |
| Pain   |                  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Dysphagia                                       |                 |  |  |
| subjects affected / exposed                     | 6 / 185 (3.24%) |  |  |
| occurrences causally related to treatment / all | 0 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Pelvic pain                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Acute respiratory failure                       |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Chronic respiratory failure                     |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dyspnoea  |                 |  |  |
| subjects affected / exposed                     | 5 / 185 (2.70%) |  |  |
| occurrences causally related to treatment / all | 0 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Lung disorder                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Pleural effusion                                |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory failure                             |                 |  |  |
| subjects affected / exposed                     | 5 / 185 (2.70%) |  |  |
| occurrences causally related to treatment / all | 0 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 4           |  |  |
| Restrictive pulmonary disease                   |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Completed suicide                               |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Infections and infestations                     |                 |  |  |
| Cellulitis                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia                                       |                 |  |  |
| subjects affected / exposed                     | 4 / 185 (2.16%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 2           |  |  |
| Upper respiratory tract infection               |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| COVID-19  |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Dehydration                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Diabetic ketoacidosis                           |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Hyponatraemia                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Feeding disorder                                |                 |  |  |
| subjects affected / exposed                     | 1 / 185 (0.54%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |

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

| <b>Non-serious adverse events</b>                     | MT-1186            |  |  |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 123 / 185 (66.49%) |  |  |
| Injury, poisoning and procedural complications        |                    |  |  |
| Contusion   |                    |  |  |
| subjects affected / exposed                           | 15 / 185 (8.11%)   |  |  |
| occurrences (all)                                     | 15                 |  |  |
| Fall  |                    |  |  |
| subjects affected / exposed                           | 40 / 185 (21.62%)  |  |  |
| occurrences (all)                                     | 59                 |  |  |
| Nervous system disorders                              |                    |  |  |
| Headache  |                    |  |  |
| subjects affected / exposed                           | 13 / 185 (7.03%)   |  |  |
| occurrences (all)                                     | 18                 |  |  |
| General disorders and administration site conditions  |                    |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 14 / 185 (7.57%)<br>14  |  |  |
| Gastrointestinal disorders  |                         |  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)            | 33 / 185 (17.84%)<br>33 |  |  |
| Dysphagia<br>subjects affected / exposed<br>occurrences (all)               | 16 / 185 (8.65%)<br>17  |  |  |
| Salivary Hypersecretion<br>subjects affected / exposed<br>occurrences (all) | 11 / 185 (5.95%)<br>11  |  |  |
| Respiratory, thoracic and mediastinal disorders                             |                         |  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                | 16 / 185 (8.65%)<br>19  |  |  |
| Skin and subcutaneous tissue disorders                                      |                         |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                    | 10 / 185 (5.41%)<br>12  |  |  |
| Psychiatric disorders   |                         |  |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)              | 10 / 185 (5.41%)<br>10  |  |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                | 16 / 185 (8.65%)<br>17  |  |  |
| Musculoskeletal and connective tissue disorders                             |                         |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)               | 19 / 185 (10.27%)<br>19 |  |  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)           | 13 / 185 (7.03%)<br>14  |  |  |
| Muscular weakness   |                         |  |  |



|                             |                   |  |  |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 39 / 185 (21.08%) |  |  |
| occurrences (all)           | 60                |  |  |
| Musculoskeletal pain        |                   |  |  |
| subjects affected / exposed | 10 / 185 (5.41%)  |  |  |
| occurrences (all)           | 11                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 23 December 2019  | Significant changes included in this amendment are summarized below: <ul style="list-style-type: none"><li>• Provided additional information to clinical sites regarding dosing cycles/study days</li><li>• Clarified discrepancies within the protocol</li><li>• Corrected formatting and spelling throughout</li></ul>   |
| 26 February 2020  | The amendment clarified discrepancies within the protocol and corrected formatting and spelling throughout.  |
| 23 September 2020 | Significant changes included in this amendment are summarized below: <ul style="list-style-type: none"><li>• Updated with impacts of COVID-19, including delayed completion date, and risks and precautions taken</li><li>• Clarified discrepancies within the protocol</li><li>• Updated personnel information</li><li>• Updated introduction with information from recent studies</li><li>• Updated with current and revised guidelines</li><li>• Corrected formatting and spelling throughout</li></ul>   |
| 16 April 2021     | Significant changes included in this amendment are summarized below: <ul style="list-style-type: none"><li>• Contraceptive guidance in Appendix 2 was updated to align with the Germany-specific protocol.</li><li>• Editorial changes were made to allow PEG/RIG dosing.</li><li>• The sample size was increased to compensate for potential increased premature terminations due to COVID-19, to ensure at least 100 completers at 48 weeks of treatment.</li><li>• Due to COVID-19 restrictions related to site visits, it was clarified that formal telehealth would not be used, but instead home nursing visits or telephone calls for questionnaires would be conducted.</li><li>• It was clarified that any combination of phenylbutyrate and tauroursodeoxycholic acid was prohibited throughout the study.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported