



## Clinical trial results:

### A Phase 3, Open-Label, Multi-Center Trial to Evaluate the Long-Term Safety and Efficacy of Repeat Treatments of DaxibotulinumtoxinA for Injection in Adults with Isolated Cervical Dystonia (ASPEN-OLS)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-000447-11 |
| Trial protocol           | GB AT PL IT    |
| Global end of trial date | 25 May 2021    |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 04 May 2023  |
| First version publication date | 04 May 2023  |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | 1720304 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03617367 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Revance Therapeutics Inc   |
| Sponsor organisation address | 7555 Gateway Boulevard, Newark, California, United States, 94560                                       |
| Public contact               | Regulatory Affairs Manager, Revance Therapeutics Inc, +1 5107423557, jlintao@revance.com               |
| Scientific contact           | Senior Director, Clinical Development, Revance Therapeutics Inc, +1 5107423400, dvitarella@revance.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                       | 25 May 2021 |
| Is this the analysis of the primary completion data? | No          |

|                                  |             |
|----------------------------------|-------------|
| Global end of trial reached?     | Yes         |
| Global end of trial date         | 25 May 2021 |
| Was the trial ended prematurely? | No          |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the long-term safety of multiple continuous treatments of daxibotulinumtoxinA (DAXI) for injection and to assess immunogenicity to botulinum neurotoxin type A (BoNTA) and revance novel excipient (RTP004) after multiple treatments of DAXI for injection.

Protection of trial subjects:

This study was conducted in accordance with the accepted version of the Declaration of Helsinki, in compliance with International Council for Harmonisation (ICH), Good Clinical Practice (GCP) guidelines, and according to the appropriate regulatory requirements in the countries where the study was conducted.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 05 September 2018 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 65         |
| Country: Number of subjects enrolled | Spain: 12          |
| Country: Number of subjects enrolled | United Kingdom: 6  |
| Country: Number of subjects enrolled | Austria: 1         |
| Country: Number of subjects enrolled | Czechia: 26        |
| Country: Number of subjects enrolled | France: 8          |
| Country: Number of subjects enrolled | Germany: 18        |
| Country: Number of subjects enrolled | Canada: 1          |
| Country: Number of subjects enrolled | United States: 220 |
| Worldwide total number of subjects   | 357                |
| EEA total number of subjects         | 130                |

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)                     | 240 |
| From 65 to 84 years                      | 117 |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 64 sites in 9 countries (Austria, Canada, Czech Republic, France, Germany, Poland, Spain, United Kingdom, and the United States from 05 September 2018 to 25 May 2021. A total of 387 subjects were screened and 357 subjects were enrolled.

### Pre-assignment

Screening details:

A total of 387 subjects were screened, of which 357 subjects were enrolled and treated. Few subjects had multiple movement within the arms in the treatment cycles so, only overall subjects data was planned, analysed and reported to avoid double-counting in disposition and baseline.

### Period 1

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

### Arms

|           |                            |
|-----------|----------------------------|
| Arm title | DaxibotulinumtoxinA (DAXI) |
|-----------|----------------------------|

Arm description:

Subjects received 4 continuous treatments of multi-dose of DAXI intramuscular (IM) injection (125 U, 200 U, 250 U, and 300 U). In cycle 1 subjects received DAXI IM injection (DAXI 125 U or 250 U) based on clinical factors, CD disease severity, and prior BoNT treatment history, using the dose selection criteria on Day 1. In treatment cycles 2 to 4, subjects received same DAXI dose received in cycle 1 (125 U or 250 U), or there was an increase or decrease in the DAXI dose by 1 predefined dose step per subsequent cycle based on the subject's treatment response in the prior cycle, as determined by the Investigator. The 2 additional DAXI doses for these dose steps were started in cycle 2: DAXI 200 U and DAXI 300 U. If subjects had received retreatment at 12 weeks during each of the first 2 cycles, a 3rd cycle could not have a duration greater than 28 weeks, and if subjects had received 12 weeks of treatment during each of the first 3 cycles, a 4 cycle could not go longer than 16 weeks.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | DAXI                   |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Subjects received 4 multi-dose of DAXI IM injection (125 U, 200 U, 250 U, and 300 U).

| Number of subjects in period 1 | DaxibotulinumtoxinA (DAXI) |
|--------------------------------|----------------------------|
| Started                        | 357                        |
| Treatment Cycle 1              | 357                        |
| Treatment Cycle 2              | 329                        |
| Treatment Cycle 3              | 234 <sup>[1]</sup>         |
| Treatment Cycle 4              | 65 <sup>[2]</sup>          |
| Completed                      | 297                        |
| Not completed                  | 60                         |

|                              |    |
|------------------------------|----|
| Consent withdrawn by subject | 15 |
| Adverse Event                | 2  |
| Protocol violation           | 6  |
| Death                        | 1  |
| Other                        | 2  |
| Lost to follow-up            | 6  |
| Progressive disease          | 4  |
| Lack of efficacy             | 24 |

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Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Few subjects had multiple movement within the arms in the treatment cycles.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Few subjects had multiple movement within the arms in the treatment cycles.

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

Subjects received 4 continuous treatments of multi-dose of DAXI intramuscular (IM) injection (125 U, 200 U, 250 U, and 300 U). In cycle 1 subjects received DAXI IM injection (DAXI 125 U or 250 U) based on clinical factors, CD disease severity, and prior BoNT treatment history, using the dose selection criteria on Day 1. In treatment cycles 2 to 4, subjects received same DAXI dose received in cycle 1 (125 U or 250 U), or there was an increase or decrease in the DAXI dose by 1 predefined dose step per subsequent cycle based on the subject's treatment response in the prior cycle, as determined by the Investigator. The 2 additional DAXI doses for these dose steps were started in cycle 2: DAXI 200 U and DAXI 300 U. If subjects had received retreatment at 12 weeks during each of the first 2 cycles, a 3rd cycle could not have a duration greater than 28 weeks, and if subjects had received 12 weeks of treatment during each of the first 3 cycles, a 4 cycle could not go longer than 16 weeks.

| Reporting group values | Overall Study | Total |  |
|------------------------|---------------|-------|--|
| Number of subjects     | 357           | 357   |  |
| Age categorical        |               |       |  |
| Units: Subjects        |               |       |  |

|   |         |     |  |
|---|---------|-----|--|
| Age continuous                            |         |     |  |
| Units: years                              |         |     |  |
| arithmetic mean                           | 57.6    |     |  |
| standard deviation                        | ± 11.86 | -   |  |
| Gender categorical                        |         |     |  |
| Units: Subjects                           |         |     |  |
| Female                                    | 238     | 238 |  |
| Male                                      | 119     | 119 |  |
| Race                                      |         |     |  |
| Units: Subjects                           |         |     |  |
| White                                     | 342     | 342 |  |
| Black                                     | 6       | 6   |  |
| Asian                                     | 4       | 4   |  |
| American Indian or Alaska Native          | 1       | 1   |  |
| Native Hawaiian or other Pacific Islander | 1       | 1   |  |
| Other                                     | 3       | 3   |  |
| Ethnicity                                 |         |     |  |
| Units: Subjects                           |         |     |  |
| Hispanic or Latino                        | 19      | 19  |  |
| Not Hispanic or Latino                    | 333     | 333 |  |
| Not provided                              | 5       | 5   |  |

## End points

### End points reporting groups

|   |                               |
|---|-------------------------------|
| Reporting group title   | DaxibotulinumtoxinA (DAXI)    |
| Reporting group description:<br>Subjects received 4 continuous treatments of multi-dose of DAXI intramuscular (IM) injection (125 U, 200 U, 250 U, and 300 U). In cycle 1 subjects received DAXI IM injection (DAXI 125 U or 250 U) based on clinical factors, CD disease severity, and prior BoNT treatment history, using the dose selection criteria on Day 1. In treatment cycles 2 to 4, subjects received same DAXI dose received in cycle 1 (125 U or 250 U), or there was an increase or decrease in the DAXI dose by 1 predefined dose step per subsequent cycle based on the subject's treatment response in the prior cycle, as determined by the Investigator. The 2 additional DAXI doses for these dose steps were started in cycle 2: DAXI 200 U and DAXI 300 U. If subjects had received retreatment at 12 weeks during each of the first 2 cycles, a 3rd cycle could not have a duration greater than 28 weeks, and if subjects had received 12 weeks of treatment during each of the first 3 cycles, a 4 cycle could not go longer than 16 weeks. |                               |
| Subject analysis set title  | Treatment Cycle 1: DAXI 125 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 125 U solution, IM injection in treatment cycle 1.  |                               |
| Subject analysis set title  | Treatment Cycle 2: DAXI 125 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 125 U solution, IM injection in treatment cycle 2.  |                               |
| Subject analysis set title  | Treatment Cycle 3: DAXI 125 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 125 U solution, IM injection in treatment cycle 3.  |                               |
| Subject analysis set title  | Treatment Cycle 4: DAXI 125 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 125 U solution, IM injection in treatment cycle 4.  |                               |
| Subject analysis set title  | Treatment Cycle 2: DAXI 200 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 200 U solution, IM injection in treatment cycle 2.  |                               |
| Subject analysis set title  | Treatment Cycle 3: DAXI 200 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 200 U solution, IM injection in treatment cycle 3.  |                               |
| Subject analysis set title  | Treatment Cycle 4: DAXI 200 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 200 U solution, IM injection in treatment cycle 4.  |                               |
| Subject analysis set title  | Treatment Cycle 1: DAXI 250 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 250 U solution, IM injection in treatment cycle 1.  |                               |
| Subject analysis set title  | Treatment Cycle 2: DAXI 250 U |
| Subject analysis set type   | Safety analysis               |
| Subject analysis set description:<br>Subjects received DAXI 250 U solution, IM injection in treatment cycle 2.  |                               |
| Subject analysis set title  | Treatment Cycle 3: DAXI 250 U |
| Subject analysis set type   | Safety analysis               |

Subject analysis set description:

Subjects received DAXI 250 U solution, IM injection in treatment cycle 3.

|                            |                               |
|----------------------------|-------------------------------|
| Subject analysis set title | Treatment Cycle 4: DAXI 250 U |
| Subject analysis set type  | Safety analysis               |

Subject analysis set description:

Subjects received DAXI 250 U solution, IM injection in treatment cycle 4.

|                            |                               |
|----------------------------|-------------------------------|
| Subject analysis set title | Treatment Cycle 2: DAXI 300 U |
| Subject analysis set type  | Safety analysis               |

Subject analysis set description:

Subjects received DAXI 300 U solution, IM injection in treatment cycle 2.

|                            |                               |
|----------------------------|-------------------------------|
| Subject analysis set title | Treatment Cycle 3: DAXI 300 U |
| Subject analysis set type  | Safety analysis               |

Subject analysis set description:

Subjects received DAXI 300 U solution, IM injection in treatment cycle 3.

|                            |                               |
|----------------------------|-------------------------------|
| Subject analysis set title | Treatment Cycle 4: DAXI 300 U |
| Subject analysis set type  | Safety analysis               |

Subject analysis set description:

Subjects received DAXI 300 U solution, IM injection in treatment cycle 4.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Treatment Cycle 1 Total |
| Subject analysis set type  | Safety analysis         |

Subject analysis set description:

Total number of subjects who received treatment (DAXI 125U or DAXI 250U) in Cycle 1.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Treatment Cycle 2 Total |
| Subject analysis set type  | Safety analysis         |

Subject analysis set description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in Cycle 2.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Treatment Cycle 3 Total |
| Subject analysis set type  | Safety analysis         |

Subject analysis set description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in cycle 3.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Treatment Cycle 4 Total |
| Subject analysis set type  | Safety analysis         |

Subject analysis set description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in cycle 4.

### **Primary: Number of Subjects with Drug-related Treatment-emergent Adverse Events (TEAEs) and Study Drug Discontinuation due to Drug-related TEAEs**

|                 |  |
|-----------------|--|
| End point title | Number of Subjects with Drug-related Treatment-emergent Adverse Events (TEAEs) and Study Drug Discontinuation due to Drug-related TEAEs <sup>[1]</sup> |
|-----------------|--|

End point description:

An AE was defined as any untoward medical occurrence (e.g., sign, symptom, disease, syndrome, intercurrent illness, clinically significant abnormal laboratory finding, injury, or accident) that emerged or worsened following administration of the study drug; AEs were recorded until the end of study participation. The untoward medical occurrence may not necessarily have had a causal relationship to the administration of the study drug. A TEAE was one that occurred after any exposure to study drug. Number of subjects with drug-related TEAEs and study drug discontinuation due to drug-related TEAEs were reported. Safety population was defined as all enrolled subjects who receive at least one dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to Week 52



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: Only descriptive data was planned to be analysed for this endpoint.

| End point values                            | Treatment Cycle 1 Total | Treatment Cycle 2 Total | Treatment Cycle 3 Total | Treatment Cycle 4 Total |
|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                          | Subject analysis set    | Subject analysis set    | Subject analysis set    | Subject analysis set    |
| Number of subjects analysed                 | 357                     | 329                     | 234                     | 65                      |
| Units: subjects                             |                         |                         |                         |                         |
| number (not applicable)                     |                         |                         |                         |                         |
| Any treatment-related TEAE                  | 75                      | 56                      | 46                      | 9                       |
| TEAE that led to study drug discontinuation | 1                       | 0                       | 2                       | 0                       |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects who Developed Anti-drug Antibodies (ADAs) to RTP004 by Treatment Cycles and Dose

|                 |  |
|-----------------|--|
| End point title | Number of Subjects who Developed Anti-drug Antibodies (ADAs) to RTP004 by Treatment Cycles and Dose <sup>[2]</sup> |
|-----------------|--|

End point description:

Subjects who developed ADAs (negative and positive) to analyte RTP004 were reported. Positive ADAs consisted of Treatment-induced, treatment unaffected, and treatment-boosted RTP004 ADAs. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to Week 52

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: Only descriptive data was planned to be analysed for this endpoint.

| End point values                            | Treatment Cycle 1: DAXI 125 U | Treatment Cycle 2: DAXI 125 U | Treatment Cycle 3: DAXI 125 U | Treatment Cycle 4: DAXI 125 U |
|---|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type                          | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed                 | 109                           | 43                            | 16                            | 1                             |
| Units: subjects                             |                               |                               |                               |                               |
| Treatment-induced ADA                       | 0                             | 0                             | 0                             | 0                             |
| Treatment-unaffected ADA                    | 1                             | 0                             | 0                             | 0                             |
| Treatment-boosted ADA                       | 0                             | 0                             | 0                             | 0                             |
| ADA-negative and treatment-induced negative | 108                           | 43                            | 16                            | 1                             |

| End point values | Treatment Cycle 2: DAXI 200 U | Treatment Cycle 3: DAXI 200 U | Treatment Cycle 4: DAXI 200 U | Treatment Cycle 1: DAXI 250 U |
|------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
|------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|

| Subject group type                          | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
|---|----------------------|----------------------|----------------------|----------------------|
| Number of subjects analysed                 | 68                   | 29                   | 10                   | 234                  |
| Units: subjects                             |                      |                      |                      |                      |
| Treatment-induced ADA                       | 1                    | 0                    | 0                    | 2                    |
| Treatment-unaffected ADA                    | 1                    | 1                    | 0                    | 3                    |
| Treatment-boosted ADA                       | 0                    | 0                    | 0                    | 0                    |
| ADA-negative and treatment-induced negative | 66                   | 28                   | 10                   | 229                  |

| End point values                            | Treatment<br>Cycle 2: DAXI<br>250 U | Treatment<br>Cycle 3: DAXI<br>250 U | Treatment<br>Cycle 4: DAXI<br>250 U | Treatment<br>Cycle 2: DAXI<br>300 U |
|---|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                          | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed                 | 103                                 | 87                                  | 15                                  | 102                                 |
| Units: subjects                             |                                     |                                     |                                     |                                     |
| Treatment-induced ADA                       | 0                                   | 1                                   | 0                                   | 0                                   |
| Treatment-unaffected ADA                    | 2                                   | 2                                   | 0                                   | 1                                   |
| Treatment-boosted ADA                       | 0                                   | 0                                   | 0                                   | 0                                   |
| ADA-negative and treatment-induced negative | 101                                 | 84                                  | 15                                  | 101                                 |

| End point values                            | Treatment<br>Cycle 3: DAXI<br>300 U | Treatment<br>Cycle 4: DAXI<br>300 U |  |  |
|---|-------------------------------------|-------------------------------------|--|--|
| Subject group type                          | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed                 | 98                                  | 38                                  |  |  |
| Units: subjects                             |                                     |                                     |  |  |
| Treatment-induced ADA                       | 1                                   | 0                                   |  |  |
| Treatment-unaffected ADA                    | 2                                   | 2                                   |  |  |
| Treatment-boosted ADA                       | 0                                   | 0                                   |  |  |
| ADA-negative and treatment-induced negative | 95                                  | 36                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects who Developed Anti-drug Antibodies (ADAs) to RTT150 by Treatment Cycles and Dose

|   |  |
|---|--|
| End point title   | Number of Subjects who Developed Anti-drug Antibodies (ADAs) to RTT150 by Treatment Cycles and Dose <sup>[3]</sup> |
| End point description:  |  |
| Subjects who developed ADAs (negative and positive) to analyte RTT150 were reported. Positive ADAs consisted of Treatment-induced, treatment unaffected, and treatment-boosted RTT150 ADAs. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint. |  |
| End point type  | Primary  |

End point timeframe:

Baseline up to Week 52

Notes:

[3] - 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: Only descriptive data was planned to be analysed for this endpoint.

| End point values                               | Treatment<br>Cycle 1: DAXI<br>125 U | Treatment<br>Cycle 2: DAXI<br>125 U | Treatment<br>Cycle 3: DAXI<br>125 U | Treatment<br>Cycle 4: DAXI<br>125 U |
|--|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                             | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed                    | 109                                 | 43                                  | 16                                  | 1                                   |
| Units: subjects                                |                                     |                                     |                                     |                                     |
| Treatment-induced ADA                          | 1                                   | 0                                   | 0                                   | 0                                   |
| Treatment-unaffected ADA                       | 2                                   | 1                                   | 1                                   | 0                                   |
| Treatment-boosted ADA                          | 0                                   | 0                                   | 0                                   | 0                                   |
| ADA-negative and treatment-induced<br>negative | 106                                 | 42                                  | 15                                  | 1                                   |

| End point values                               | Treatment<br>Cycle 2: DAXI<br>200 U | Treatment<br>Cycle 3: DAXI<br>200 U | Treatment<br>Cycle 4: DAXI<br>200 U | Treatment<br>Cycle 1: DAXI<br>250 U |
|--|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                             | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed                    | 69                                  | 29                                  | 10                                  | 237                                 |
| Units: subjects                                |                                     |                                     |                                     |                                     |
| Treatment-induced ADA                          | 1                                   | 0                                   | 0                                   | 0                                   |
| Treatment-unaffected ADA                       | 1                                   | 0                                   | 0                                   | 5                                   |
| Treatment-boosted ADA                          | 0                                   | 0                                   | 0                                   | 1                                   |
| ADA-negative and treatment-induced<br>negative | 67                                  | 29                                  | 10                                  | 231                                 |

| End point values                               | Treatment<br>Cycle 2: DAXI<br>250 U | Treatment<br>Cycle 3: DAXI<br>250 U | Treatment<br>Cycle 4: DAXI<br>250 U | Treatment<br>Cycle 2: DAXI<br>300 U |
|--|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                             | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed                    | 103                                 | 88                                  | 15                                  | 104                                 |
| Units: subjects                                |                                     |                                     |                                     |                                     |
| Treatment-induced ADA                          | 1                                   | 1                                   | 1                                   | 0                                   |
| Treatment-unaffected ADA                       | 3                                   | 3                                   | 0                                   | 3                                   |
| Treatment-boosted ADA                          | 1                                   | 1                                   | 0                                   | 0                                   |
| ADA-negative and treatment-induced<br>negative | 98                                  | 83                                  | 14                                  | 101                                 |

| End point values            | Treatment<br>Cycle 3: DAXI<br>300 U | Treatment<br>Cycle 4: DAXI<br>300 U |  |  |
|-----------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type          | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed | 100                                 | 39                                  |  |  |

|   |    |    |  |  |
|---|----|----|--|--|
| Units: subjects                             |    |    |  |  |
| Treatment-induced ADA                       | 0  | 0  |  |  |
| Treatment-unaffected ADA                    | 2  | 2  |  |  |
| Treatment-boosted ADA                       | 0  | 0  |  |  |
| ADA-negative and treatment-induced negative | 98 | 37 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects who Developed Neutralizing Anti-drug Antibodies (ADAs) to RTT150 by Treatment Cycles and Dose

|                 |   |
|-----------------|---|
| End point title | Number of Subjects who Developed Neutralizing Anti-drug Antibodies (ADAs) to RTT150 by Treatment Cycles and Dose <sup>[4]</sup> |
|-----------------|---|

End point description:

Subjects who developed NABs (negative and positive) to analyte RTT150 were reported. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Treatment Cycle 1: Up to Week 36, Treatment Cycle 2: Up to Week 28, Treatment Cycle 3: Up to Week 16 and Treatment Cycle 4: Up to Week 16

Notes:

[4] - 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: Only descriptive data was planned to be analysed for this endpoint.

| End point values            | Treatment Cycle 1: DAXI 125 U | Treatment Cycle 2: DAXI 125 U | Treatment Cycle 3: DAXI 125 U | Treatment Cycle 4: DAXI 125 U |
|-----------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type          | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed | 0 <sup>[5]</sup>              | 0 <sup>[6]</sup>              | 0 <sup>[7]</sup>              | 0 <sup>[8]</sup>              |
| Units: Subjects             |                               |                               |                               |                               |
| NAb positive                |                               |                               |                               |                               |
| NAb negative                |                               |                               |                               |                               |

Notes:

[5] - No subjects were analysed at this timepoint (Week 36).

[6] - No subjects were analysed at this timepoint (Week 28).

[7] - No subjects were analysed at this timepoint (Week 16).

[8] - No subjects were analysed at this timepoint (Week 16).

| End point values            | Treatment Cycle 2: DAXI 200 U | Treatment Cycle 3: DAXI 200 U | Treatment Cycle 4: DAXI 200 U | Treatment Cycle 1: DAXI 250 U |
|-----------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type          | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed | 0 <sup>[9]</sup>              | 0 <sup>[10]</sup>             | 0 <sup>[11]</sup>             | 1                             |
| Units: Subjects             |                               |                               |                               |                               |
| NAb positive                |                               |                               |                               | 0                             |
| NAb negative                |                               |                               |                               | 1                             |

Notes:

[9] - No subjects were analysed at this timepoint (Week 28).

[10] - No subjects were analysed at this timepoint (Week 16).

[11] - No subjects were analysed at this timepoint (Week 16).

| End point values            | Treatment<br>Cycle 2: DAXI<br>250 U | Treatment<br>Cycle 3: DAXI<br>250 U | Treatment<br>Cycle 4: DAXI<br>250 U | Treatment<br>Cycle 2: DAXI<br>300 U |
|-----------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type          | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed | 1                                   | 1                                   | 0 <sup>[12]</sup>                   | 0 <sup>[13]</sup>                   |
| Units: Subjects             |                                     |                                     |                                     |                                     |
| NAb positive                | 1                                   | 1                                   |                                     |                                     |
| NAb negative                | 0                                   | 0                                   |                                     |                                     |

Notes:

[12] - No subjects were analysed at this timepoint (Week 16).

[13] - No subjects were analysed at this timepoint (Week 28).

| End point values            | Treatment<br>Cycle 3: DAXI<br>300 U | Treatment<br>Cycle 4: DAXI<br>300 U |  |  |
|-----------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type          | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed | 0 <sup>[14]</sup>                   | 1                                   |  |  |
| Units: Subjects             |                                     |                                     |  |  |
| NAb positive                |                                     | 1                                   |  |  |
| NAb negative                |                                     | 0                                   |  |  |

Notes:

[14] - No subjects were analysed at this timepoint (Week 16).

## Statistical analyses

No statistical analyses for this end point

## Secondary: Average Change from Baseline in Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) Total Score at Weeks 4 and 6 by Treatment Cycles and Dose

|                 |   |
|-----------------|---|
| End point title | Average Change from Baseline in Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) Total Score at Weeks 4 and 6 by Treatment Cycles and Dose |
|-----------------|---|

End point description:

The TWSTRS was an assessment scale used to measure the impact of CD on subjects and comprises 3 subscales: Severity (0–35), disability (0–30) and pain (0–20), each of which was scored independently. The total score from the 3 subscales gives the TWSTRS total score with a value from 0 to 85 (best to worst). The higher score indicates worst outcomes, and a negative change indicates better outcomes. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint. Here "99999" refers to data not available and we have added it as space-fillers.

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

End point timeframe:

Baseline, Week 4 and 6

| End point values                     | Treatment Cycle 1: DAXI 125 U | Treatment Cycle 2: DAXI 125 U | Treatment Cycle 3: DAXI 125 U | Treatment Cycle 4: DAXI 125 U |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type                   | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed          | 107                           | 41                            | 15                            | 1                             |
| Units: Score on scale                |                               |                               |                               |                               |
| arithmetic mean (standard deviation) | -15.0 (± 10.43)               | -15.6 (± 12.26)               | -15.0 (± 11.55)               | -9.7 (± 99999)                |

| End point values                     | Treatment Cycle 2: DAXI 200 U | Treatment Cycle 3: DAXI 200 U | Treatment Cycle 4: DAXI 200 U | Treatment Cycle 1: DAXI 250 U |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type                   | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed          | 71                            | 29                            | 8                             | 243                           |
| Units: Score on scale                |                               |                               |                               |                               |
| arithmetic mean (standard deviation) | -19.5 (± 10.34)               | -19.6 (± 11.07)               | -13.9 (± 11.31)               | -15.6 (± 10.26)               |

| End point values                     | Treatment Cycle 2: DAXI 250 U | Treatment Cycle 3: DAXI 250 U | Treatment Cycle 4: DAXI 250 U | Treatment Cycle 2: DAXI 300 U |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type                   | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed          | 100                           | 87                            | 14                            | 103                           |
| Units: Score on scale                |                               |                               |                               |                               |
| arithmetic mean (standard deviation) | -19.9 (± 10.78)               | -18.1 (± 10.99)               | -21.4 (± 12.63)               | -15.2 (± 11.67)               |

| End point values                     | Treatment Cycle 3: DAXI 300 U | Treatment Cycle 4: DAXI 300 U |  |  |
|--------------------------------------|-------------------------------|-------------------------------|--|--|
| Subject group type                   | Subject analysis set          | Subject analysis set          |  |  |
| Number of subjects analysed          | 96                            | 39                            |  |  |
| Units: Score on scale                |                               |                               |  |  |
| arithmetic mean (standard deviation) | -17.5 (± 11.71)               | -20.9 (± 14.31)               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Effect (Time to Loss of Efficacy Based on TWSTRS Total Score) by Treatment Cycles and Dose

|                 |  |
|-----------------|--|
| End point title | Duration of Effect (Time to Loss of Efficacy Based on TWSTRS Total Score) by Treatment Cycles and Dose |
|-----------------|--|

End point description:

The duration of effect was defined as the time in weeks after each treatment until loss of at least 80% of

the peak treatment effect based on TWSTRS total score (loss of efficacy). The peak treatment effect was defined as the average change from baseline at Weeks 4 and 6 in the TWSTRS total score. Duration of effect is only evaluable in Cycles 1 and 2; due to the 52-week limit on study participation, Cycles 3 and 4 are artificially truncated and therefore not provided valid estimates of duration. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here "99999" refers to data not available and we have added it as space-fillers. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline, Week 4 and 6 |           |

| End point values                 | Treatment Cycle 1: DAXI 125 U | Treatment Cycle 2: DAXI 125 U | Treatment Cycle 2: DAXI 200 U | Treatment Cycle 1: DAXI 250 U |
|----------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type               | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed      | 111                           | 44                            | 71                            | 246                           |
| Units: weeks                     |                               |                               |                               |                               |
| median (confidence interval 95%) | 21.3 (19.3 to 24.4)           | 26.0 (20.1 to 32.1)           | 21.0 (19.0 to 24.0)           | 19.9 (17.1 to 20.9)           |

| End point values                 | Treatment Cycle 2: DAXI 250 U | Treatment Cycle 2: DAXI 300 U |  |  |
|----------------------------------|-------------------------------|-------------------------------|--|--|
| Subject group type               | Subject analysis set          | Subject analysis set          |  |  |
| Number of subjects analysed      | 107                           | 107                           |  |  |
| Units: weeks                     |                               |                               |  |  |
| median (confidence interval 95%) | 20.1 (17.1 to 28.1)           | 20.1 (17.7 to 24.4)           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with at least "moderate" (a 2-point) improvement on Clinical Global Impression of Change (CGIC) at Week 4 or Week 6 of Each Treatment Cycle

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects with at least "moderate" (a 2-point) improvement on Clinical Global Impression of Change (CGIC) at Week 4 or Week 6 of Each Treatment Cycle |
|-----------------|--|

End point description:

The CGIC was a questionnaire that captures the clinician's overall impression of the subject's response to study treatment. The clinician's selected response maps to a 7-point scale: -3 (very much worse), 0 (about the same), to +3 (very much better). The higher score indicates better outcomes. A 2+ point improvement was defined as a response of moderately better (+2) or very much better (+3) at Week 4 or Week 6. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| At Week 4 or 6       |           |

| <b>End point values</b>       | Treatment<br>Cycle 1: DAXI<br>125 U | Treatment<br>Cycle 2: DAXI<br>125 U | Treatment<br>Cycle 3: DAXI<br>125 U | Treatment<br>Cycle 4: DAXI<br>125 U |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed   | 109                                 | 42                                  | 15                                  | 1                                   |
| Units: Percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 75.7                                | 79.5                                | 75.0                                | 100                                 |

| <b>End point values</b>       | Treatment<br>Cycle 2: DAXI<br>200 U | Treatment<br>Cycle 3: DAXI<br>200 U | Treatment<br>Cycle 4: DAXI<br>200 U | Treatment<br>Cycle 1: DAXI<br>250 U |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed   | 71                                  | 29                                  | 8                                   | 244                                 |
| Units: Percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 84.5                                | 90.0                                | 80.0                                | 70.7                                |

| <b>End point values</b>       | Treatment<br>Cycle 2: DAXI<br>250 U | Treatment<br>Cycle 3: DAXI<br>250 U | Treatment<br>Cycle 4: DAXI<br>250 U | Treatment<br>Cycle 2: DAXI<br>300 U |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Subject analysis set                | Subject analysis set                | Subject analysis set                | Subject analysis set                |
| Number of subjects analysed   | 103                                 | 87                                  | 14                                  | 104                                 |
| Units: Percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 86.0                                | 77.3                                | 80.0                                | 76.6                                |

| <b>End point values</b>       | Treatment<br>Cycle 3: DAXI<br>300 U | Treatment<br>Cycle 4: DAXI<br>300 U |  |  |
|-------------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type            | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed   | 96                                  | 39                                  |  |  |
| Units: Percentage of subjects |                                     |                                     |  |  |
| number (not applicable)       | 76.0                                | 84.6                                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects with at least "moderate" (a 2-point) improvement on Patient Global Impression of Change (PGIC) at Week 4 or Week 6 of Each Treatment Cycle

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects with at least "moderate" (a 2-point) improvement on Patient Global Impression of Change (PGIC) at |
|-----------------|--|



End point description:

The PGIC was a questionnaire that captures the patient's overall impression of their response to study treatment. The subject's selected response maps to a 7-point scale: -3 (very much worse), 0 (about the same), to +3 (very much better). A 2+ point improvement was defined as a response of moderately better (+2) or very much better (+3) at Week 4 or Week 6. The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "number of subjects analysed" refer to the subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

At Week 4 or 6

| End point values              | Treatment Cycle 1: DAXI 125 U | Treatment Cycle 2: DAXI 125 U | Treatment Cycle 3: DAXI 125 U | Treatment Cycle 4: DAXI 125 U |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type            | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed   | 109                           | 42                            | 15                            | 1                             |
| Units: Percentage of subjects |                               |                               |                               |                               |
| number (not applicable)       | 69.4                          | 68.2                          | 43.8                          | 100                           |

| End point values              | Treatment Cycle 2: DAXI 200 U | Treatment Cycle 3: DAXI 200 U | Treatment Cycle 4: DAXI 200 U | Treatment Cycle 1: DAXI 250 U |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type            | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed   | 71                            | 29                            | 8                             | 244                           |
| Units: Percentage of subjects |                               |                               |                               |                               |
| number (not applicable)       | 80.3                          | 93.3                          | 60.0                          | 66.3                          |

| End point values              | Treatment Cycle 2: DAXI 250 U | Treatment Cycle 3: DAXI 250 U | Treatment Cycle 4: DAXI 250 U | Treatment Cycle 2: DAXI 300 U |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type            | Subject analysis set          | Subject analysis set          | Subject analysis set          | Subject analysis set          |
| Number of subjects analysed   | 103                           | 87                            | 14                            | 104                           |
| Units: Percentage of subjects |                               |                               |                               |                               |
| number (not applicable)       | 80.4                          | 68.2                          | 60.0                          | 58.9                          |

| End point values              | Treatment Cycle 3: DAXI 300 U | Treatment Cycle 4: DAXI 300 U |  |  |
|-------------------------------|-------------------------------|-------------------------------|--|--|
| Subject group type            | Subject analysis set          | Subject analysis set          |  |  |
| Number of subjects analysed   | 96                            | 39                            |  |  |
| Units: Percentage of subjects |                               |                               |  |  |
| number (not applicable)       | 57.0                          | 74.4                          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline in Quality of Life (QOL) measured based on the Cervical Dystonia Impact Profile (CDIP-58) at Week 6

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline in Quality of Life (QOL) measured based on the Cervical Dystonia Impact Profile (CDIP-58) at Week 6 |
|-----------------|--|

End point description:

The CDIP-58 assesses the health impact of CD. The CDIP-58 is composed of eight domains: head and neck (6 items; 6 to 30 points), pain and discomfort (5 items; 5 to 25 points), upper limb activities (9 items; 9 to 45 points), walking (9 items; 9 to 45 points), sleep (4 items; 4 to 20 points), annoyance (8 items; 8 to 40 points), mood (7 items; 7 to 35 points), and psychosocial functioning (10 items; 10 to 50 points). Subscale scores were transformed to a common theoretical range of 0 (no impact) to 100 (most impact). The safety population was defined as all enrolled subjects who received at least 1 dose of study drug. Here, "n= number analysed" signifies to subjects evaluable at given category.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline, Week 6     |           |

| End point values                                | Treatment Cycle 1 Total | Treatment Cycle 2 Total | Treatment Cycle 3 Total | Treatment Cycle 4 Total |
|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type                              | Subject analysis set    | Subject analysis set    | Subject analysis set    | Subject analysis set    |
| Number of subjects analysed                     | 357                     | 329                     | 234                     | 65                      |
| Units: Percent Change                           |                         |                         |                         |                         |
| arithmetic mean (standard deviation)            |                         |                         |                         |                         |
| Annoyance (n=309,273,201,56)                    | -29.46 (± 98.827)       | -49.54 (± 57.094)       | -40.35 (± 68.949)       | -49.25 (± 54.633)       |
| Head and neck symptoms (n=333,292,208,57)       | -36.83 (± 35.884)       | -46.13 (± 33.539)       | -40.19 (± 37.735)       | -48.60 (± 40.805)       |
| Mood (n=273,242,179,51)                         | -29.09 (± 93.496)       | -45.73 (± 73.222)       | -45.42 (± 68.085)       | -37.11 (± 139.591)      |
| Pain and discomfort symptoms (n=326,284,204,55) | -36.82 (± 49.805)       | -48.75 (± 48.029)       | -39.24 (± 46.514)       | -50.65 (± 37.450)       |
| Psychosocial functioning (n=302,268,200,55)     | -35.82 (± 58.520)       | -48.75 (± 48.029)       | -41.47 (± 65.214)       | -47.73 (± 46.804)       |
| Sleep (n=264,231,167,53)                        | -47.03 (± 78.131)       | -56.09 (± 52.852)       | -47.26 (± 59.372)       | -56.84 (± 55.075)       |
| Upper limb activity symptoms (n=313,277,199,56) | -26.84 (± 69.077)       | -38.20 (± 62.693)       | -36.31 (± 57.008)       | -45.91 (± 43.393)       |
| Walking (n=262,231,170,46)                      | -35.51 (± 95.256)       | -36.20 (± 105.067)      | -25.15 (± 110.519)      | -16.07 (± 128.252)      |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Cycle 1 Total |
|-----------------------|-------------------------|

Reporting group description:

Total number of subjects who received treatment (DAXI 125U or DAXI 250U) in Cycle 1.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Cycle 2 Total |
|-----------------------|-------------------------|

Reporting group description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in Cycle 2.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Cycle 3 Total |
|-----------------------|-------------------------|

Reporting group description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in Cycle 3.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Cycle 4 Total |
|-----------------------|-------------------------|

Reporting group description:

Total number of subjects who received treatment (DAXI 125 U, DAXI 200 U, DAXI 250 U or DAXI 300 U) in Cycle 4.

| Serious adverse events  | Treatment Cycle 1<br>Total | Treatment Cycle 2<br>Total | Treatment Cycle 3<br>Total |
|---|----------------------------|----------------------------|----------------------------|
| Total subjects affected by serious adverse events                   |                            |                            |                            |
| subjects affected / exposed   | 2 / 357 (0.56%)            | 6 / 329 (1.82%)            | 8 / 234 (3.42%)            |
| number of deaths (all causes)                                       | 0                          | 1                          | 0                          |
| number of deaths resulting from adverse events                      | 0                          | 1                          | 0                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                            |                            |                            |
| Breast cancer   |                            |                            |                            |
| subjects affected / exposed   | 0 / 357 (0.00%)            | 0 / 329 (0.00%)            | 1 / 234 (0.43%)            |
| occurrences causally related to treatment / all                     | 0 / 0                      | 0 / 0                      | 0 / 1                      |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                      | 0 / 0                      |
| Intraductal proliferative breast lesion                             |                            |                            |                            |
| subjects affected / exposed   | 0 / 357 (0.00%)            | 1 / 329 (0.30%)            | 0 / 234 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 0                      | 0 / 1                      | 0 / 0                      |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                      | 0 / 0                      |
| Squamous cell carcinoma of lung                                     |                            |                            |                            |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 357 (0.00%) | 0 / 329 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications       |                 |                 |                 |
| Accidental overdose                                  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 357 (0.00%) | 0 / 329 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Fall   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 357 (0.00%) | 1 / 329 (0.30%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Head injury  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 357 (0.00%) | 0 / 329 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                             |                 |                 |                 |
| Intracranial aneurysm                                |                 |                 |                 |
| subjects affected / exposed                          | 1 / 357 (0.28%) | 0 / 329 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders                 |                 |                 |                 |
| Blood loss anaemia                                   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 357 (0.00%) | 1 / 329 (0.30%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                 |                 |                 |
| Non-cardiac chest pain                               |                 |                 |                 |
| subjects affected / exposed                          | 1 / 357 (0.28%) | 0 / 329 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                           |                 |                 |                 |
| Hiatus hernia  |                 |                 |                 |

|   |                            |                 |                 |
|---|----------------------------|-----------------|-----------------|
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 0 / 329 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders   |                            |                 |                 |
| Pulmonary embolism                                |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 0 / 329 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                       |                            |                 |                 |
| Acute kidney injury                               |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 1 / 329 (0.30%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| Chronic kidney disease                            |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 1 / 329 (0.30%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 1           | 0 / 0           |
| Infections and infestations                       |                            |                 |                 |
| COVID-19  |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 0 / 329 (0.00%) | 2 / 234 (0.85%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| Clostridium difficile colitis                     |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 0 / 329 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| Diverticulitis                                    |                            |                 |                 |
| subjects affected / exposed                       | 0 / 357 (0.00%)            | 1 / 329 (0.30%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0           | 0 / 0           |
| <b>Serious adverse events</b>                     |                            |                 |                 |
|   | Treatment Cycle 4<br>Total |                 |                 |
| Total subjects affected by serious adverse events |                            |                 |                 |
| subjects affected / exposed                       | 1 / 65 (1.54%)             |                 |                 |

|   |                |  |  |
|---|----------------|--|--|
| number of deaths (all causes)                                       | 0              |  |  |
| number of deaths resulting from adverse events                      | 0              |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |  |  |
| Breast cancer   |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Intraductal proliferative breast lesion                             |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Squamous cell carcinoma of lung                                     |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Injury, poisoning and procedural complications                      |                |  |  |
| Accidental overdose   |                |  |  |
| subjects affected / exposed   | 1 / 65 (1.54%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 1          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Fall  |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Head injury   |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Nervous system disorders  |                |  |  |
| Intracranial aneurysm   |                |  |  |
| subjects affected / exposed   | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Blood and lymphatic system disorders                                |                |  |  |

|  |                |  |  |
|--|----------------|--|--|
| Blood loss anaemia                                   |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Non-cardiac chest pain                               |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Hiatus hernia  |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders      |                |  |  |
| Pulmonary embolism                                   |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Renal and urinary disorders                          |                |  |  |
| Acute kidney injury                                  |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Chronic kidney disease                               |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Infections and infestations                          |                |  |  |
| COVID-19   |                |  |  |
| subjects affected / exposed                          | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Clostridium difficile colitis                        |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diverticulitis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 65 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 3 %

| <b>Non-serious adverse events</b>                     | Treatment Cycle 1<br>Total | Treatment Cycle 2<br>Total | Treatment Cycle 3<br>Total |
|---|----------------------------|----------------------------|----------------------------|
| Total subjects affected by non-serious adverse events |                            |                            |                            |
| subjects affected / exposed                           | 63 / 357 (17.65%)          | 48 / 329 (14.59%)          | 40 / 234 (17.09%)          |
| Injury, poisoning and procedural complications        |                            |                            |                            |
| Fall  |                            |                            |                            |
| subjects affected / exposed                           | 5 / 357 (1.40%)            | 2 / 329 (0.61%)            | 3 / 234 (1.28%)            |
| occurrences (all)                                     | 5                          | 2                          | 3                          |
| Nervous system disorders                              |                            |                            |                            |
| Headache  |                            |                            |                            |
| subjects affected / exposed                           | 11 / 357 (3.08%)           | 9 / 329 (2.74%)            | 3 / 234 (1.28%)            |
| occurrences (all)                                     | 11                         | 9                          | 4                          |
| General disorders and administration site conditions  |                            |                            |                            |
| Injection site erythema                               |                            |                            |                            |
| subjects affected / exposed                           | 9 / 357 (2.52%)            | 6 / 329 (1.82%)            | 7 / 234 (2.99%)            |
| occurrences (all)                                     | 9                          | 6                          | 7                          |
| Injection site pain                                   |                            |                            |                            |
| subjects affected / exposed                           | 19 / 357 (5.32%)           | 9 / 329 (2.74%)            | 5 / 234 (2.14%)            |
| occurrences (all)                                     | 19                         | 10                         | 6                          |
| Gastrointestinal disorders                            |                            |                            |                            |
| Dysphagia   |                            |                            |                            |
| subjects affected / exposed                           | 15 / 357 (4.20%)           | 14 / 329 (4.26%)           | 12 / 234 (5.13%)           |
| occurrences (all)                                     | 15                         | 14                         | 12                         |
| Musculoskeletal and connective tissue disorders       |                            |                            |                            |

|                             |                  |                  |                  |
|-----------------------------|------------------|------------------|------------------|
| Arthralgia                  |                  |                  |                  |
| subjects affected / exposed | 4 / 357 (1.12%)  | 1 / 329 (0.30%)  | 0 / 234 (0.00%)  |
| occurrences (all)           | 4                | 1                | 0                |
| Muscular weakness           |                  |                  |                  |
| subjects affected / exposed | 16 / 357 (4.48%) | 17 / 329 (5.17%) | 15 / 234 (6.41%) |
| occurrences (all)           | 16               | 18               | 15               |

| <b>Non-serious adverse events</b>                     | Treatment Cycle 4<br>Total |  |  |
|---|----------------------------|--|--|
| Total subjects affected by non-serious adverse events |                            |  |  |
| subjects affected / exposed                           | 10 / 65 (15.38%)           |  |  |
| Injury, poisoning and procedural complications        |                            |  |  |
| Fall  |                            |  |  |
| subjects affected / exposed                           | 2 / 65 (3.08%)             |  |  |
| occurrences (all)                                     | 2                          |  |  |
| Nervous system disorders                              |                            |  |  |
| Headache  |                            |  |  |
| subjects affected / exposed                           | 1 / 65 (1.54%)             |  |  |
| occurrences (all)                                     | 1                          |  |  |
| General disorders and administration site conditions  |                            |  |  |
| Injection site erythema                               |                            |  |  |
| subjects affected / exposed                           | 1 / 65 (1.54%)             |  |  |
| occurrences (all)                                     | 1                          |  |  |
| Injection site pain                                   |                            |  |  |
| subjects affected / exposed                           | 2 / 65 (3.08%)             |  |  |
| occurrences (all)                                     | 2                          |  |  |
| Gastrointestinal disorders                            |                            |  |  |
| Dysphagia   |                            |  |  |
| subjects affected / exposed                           | 2 / 65 (3.08%)             |  |  |
| occurrences (all)                                     | 2                          |  |  |
| Musculoskeletal and connective tissue disorders       |                            |  |  |
| Arthralgia  |                            |  |  |
| subjects affected / exposed                           | 2 / 65 (3.08%)             |  |  |
| occurrences (all)                                     | 2                          |  |  |
| Muscular weakness                                     |                            |  |  |
| subjects affected / exposed                           | 2 / 65 (3.08%)             |  |  |
| occurrences (all)                                     | 2                          |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 02 February 2018 | <p>Protocol Amendment 1</p> <ul style="list-style-type: none"><li>•Modified Protocol title</li><li>•Changed Medical Monitor</li><li>•Modified Study design<ul style="list-style-type: none"><li>o Removed active comparator and changed dose range to fixed dose</li><li>o Changed sample size from 600 to 290 subjects</li><li>o Expanded participating countries to include Europe</li></ul></li><li>•Changed total number of sites from 50 to approximately 80 sites</li><li>•Modified the study objectives</li><li>•Modified primary, secondary, and exploratory endpoints</li><li>•Modified screening window and modified screening period from 2 to 3 weeks</li><li>•Modified schedule of assessments</li><li>•Modified Patient Global Impression of Change (PGIC) and Clinical Global Impression of Change (CGIC) scales from 9-point to 7-point scales</li><li>•Updated safety evaluations (added Spirometry and Dysphagia Severity Scale)</li><li>•Modified and updated Inclusion and exclusion criteria</li><li>•Limited dose of drug to be injected into each targeted muscle to a minimum and maximum range</li><li>•Modified scientific rationale to match updates</li><li>•Modified dose justification</li><li>•Updated the list of prohibited medications</li><li>•Modified the injectable muscles and injection volume by muscle table (Appendix A)</li><li>•Added appendices for Cervical Dystonia Impact Profile (CDIP-58), Treatment Satisfaction Questionnaire (TSQ), Work Productivity and Activity Impairment (WPAI), Questionnaire and Short Form-36 (SF-36) Survey.</li></ul> |
| 27 March 2018    | <p>Protocol Amendment 2</p> <ul style="list-style-type: none"><li>•Clarified inclusion and exclusion criteria; added 1 exclusion criterion.</li><li>•Clarified sections describing study intervention.</li><li>•Updated secondary and exploratory endpoints.</li><li>•Added more instructions for dose selection and clarified study product description.</li><li>•Clarified that subjects could discontinue study product due to safety or at any time during the study as well as when there was no treatment benefit.</li><li>•Clarified study assessment sections and moved some examples and scales to the appendices.</li><li>•Reorganized the statistical analysis section to align with headings of ICH E9 guidance.</li><li>•Added prior treatment experience, age, and gender as subgroup analyses in the exploratory endpoints.</li><li>•Made wording changes to endpoints for clarification.</li><li>•Changed sample size to approximately 300.</li><li>•Clarified muscles for injections and added mandatory parameters.</li><li>•Clarified BoNT, BoNTA and made global terminology changes for clarification: DAXI to DAXI for injection, total TWSTRS score to TWSTRS total score, medical judgment to clinical judgment.</li></ul>  |

|              |   |
|--------------|---|
| 04 June 2018 | <p>Protocol Amendment 3</p> <ul style="list-style-type: none"> <li>•Added more information about Study RT002-CL005 to the introduction.</li> <li>•Added dysphagia as a known potential risk.</li> <li>•Updated study design section for clarification.</li> <li>•Clarified and updated inclusion and exclusion criteria.</li> <li>•Updated text about allowed concomitant medications; for focal dystonia treatments, amended time for stable dose requirement from 3 months to 4 weeks.</li> <li>•Amended recruitment and retention strategies section.</li> <li>•Clarified study intervention sections.</li> <li>•Amended pregnancy section.</li> <li>•Updated UPs section to align with guidance from regulatory authorities and added suspected unexpected serious adverse reaction (SUSAR) information.</li> <li>•Clarified sections about EOS Visit, TWSTRS, AE expectedness, follow-up of nonserious AEs, and follow-up of post-study SAEs.</li> <li>•In the statistical analysis section, added objectives with endpoints and clarified efficacy endpoints.</li> <li>•Updated information for key study personnel.</li> <li>•Updated study oversight text to reflect that the Data Safety Monitoring Board (DSMB) was to review unblinded data, as this was an open-label study.</li> </ul> |
| 27 June 2018 | <p>Protocol Amendment 4</p> <ul style="list-style-type: none"> <li>•Increased sample size to approximately 350.</li> <li>•Clarified sample size justification and Increased sample size in 4.1 Overall design.</li> <li>•Clarified that a subject who has no reduction or an increase from baseline in the average TWSTRS-total score at Weeks 4 and 6 is the same as a subject who has a lack of efficacy.</li> <li>•Updated Figure 1.</li> <li>•Clarified major inclusion criteria.</li> <li>•Clarified that a subject who has no reduction or an increase from baseline in the average TWSTRS-total score at Weeks 4 and 6 is the same as a subject who has a lack of efficacy in 4.1. Overall design, and in 4.6 End of study definition and 7.2 Subject discontinuation/withdrawal from the study.</li> <li>•Updated 4.5 Justification for dose.</li> </ul>  |
| 10 July 2019 | <p>Protocol Amendment 5</p> <ul style="list-style-type: none"> <li>•Added National Clinical Trial Identified Number NCT03617367.</li> <li>•Added "Blood sample for antibody testing" at Week 4 after baseline injection and Week 4 after all retreatments.</li> <li>•Updated Medical Monitor's information.</li> </ul>  |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported