



## Clinical trial results:

### A Prospective, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Efficacy and Safety Study of Oral ELND005 for Treatment of Agitation and Aggression in Patients With Moderate to Severe Alzheimer's Disease.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-004299-20 |
| Trial protocol           | GB ES          |
| Global end of trial date | 20 May 2015    |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 30 April 2016 |
| First version publication date | 30 April 2016 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | ELND005-AG201 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01735630 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                                                                                                                                                      |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Transition Therapeutics Ireland Limited                                                                                                                                                                                              |
| Sponsor organisation address | Arthur Cox Building Earlsfort Centre, Earlsfort Terrace, Dublin, Ireland, Dublin 2                                                                                                                                                   |
| Public contact               | Aleksandra Pastrak, MD, PhD, VP, Transition Therapeutics Ireland Limited, 001 416 263 1227, <a href="mailto:apastrak@transitiontherapeutics.com">apastrak@transitiontherapeutics.com</a>                                             |
| Scientific contact           | Aleksandra Pastrak, MD, PhD, VP of Clinical Development and Medical Officer, Transition Therapeutics Ireland Limited, 001 416 263 1227, <a href="mailto:apastrak@transitiontherapeutics.com">apastrak@transitiontherapeutics.com</a> |

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                       | 30 October 2015 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 20 May 2015     |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 20 May 2015     |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of ELND005 treatment compared with placebo in reducing the severity of agitation and aggression at 12 weeks;  
To evaluate the safety and tolerability of the ELND005 dosing regimen in Moderate to Severe AD patients

Protection of trial subjects:

400 subjects planned

The study was conducted according to /ICH/ guidelines concerning Good Clinical Practice (GCP)

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 19 November 2012 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety           |
| Long term follow-up duration                              | 9 Months         |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Canada: 17         |
| Country: Number of subjects enrolled | United States: 304 |
| Country: Number of subjects enrolled | Spain: 23          |
| Country: Number of subjects enrolled | United Kingdom: 6  |
| Worldwide total number of subjects   | 350                |
| EEA total number of subjects         | 29                 |

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)      | 33  |
| From 65 to 84 years       | 280 |
| 85 years and over         | 37  |

## Subject disposition

### Recruitment

Recruitment details:

Patients recruited between Nov 2012 and Feb 2015.

### Pre-assignment

Screening details:

Patients with moderate to severe Alzheimer's Disease who had clinically significant agitation and aggression.

### Period 1

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 1 title               | Treatment period (overall period)                             |
| Is this the baseline period? | Yes                                                           |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Placebo matching ELND005

|                                        |          |
|----------------------------------------|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

PlaceboTablet - BID for 4 weeks followed by Placebo BID for 8 weeks

|                  |      |
|------------------|------|
| <b>Arm title</b> | Test |
|------------------|------|

Arm description:

ELND005 250 mg

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Scyllo Inositol |
| Investigational medicinal product code | ELND005         |
| Other name                             |                 |
| Pharmaceutical forms                   | Tablet          |
| Routes of administration               | Oral use        |

Dosage and administration details:

250mg Tablet -1000mg BID for 4 weeks followed by 250 mg BID for 8 weeks

| <b>Number of subjects in period 1</b> | Placebo | Test |
|---------------------------------------|---------|------|
| Started                               | 175     | 175  |
| Completed                             | 157     | 157  |
| Not completed                         | 18      | 18   |
| Consent withdrawn by subject          | 9       | 7    |
| Physician decision                    | 1       | -    |
| Adverse event, non-fatal              | 7       | 8    |
| Sponsor decision                      | -       | 2    |
| Sponsor decision                      | 1       | -    |
| Lost to follow-up                     | -       | 1    |

## Baseline characteristics

### Reporting groups

|                                                          |         |
|----------------------------------------------------------|---------|
| Reporting group title                                    | Placebo |
| Reporting group description:<br>Placebo matching ELND005 |         |
| Reporting group title                                    | Test    |
| Reporting group description:<br>ELND005 250 mg           |         |

| Reporting group values                | Placebo | Test   | Total |
|---------------------------------------|---------|--------|-------|
| Number of subjects                    | 175     | 175    | 350   |
| Age categorical<br>Units: Subjects    |         |        |       |
| Adults (18-64 years)                  | 20      | 13     | 33    |
| From 65-84 years                      | 132     | 142    | 274   |
| 85 years and over                     | 23      | 20     | 43    |
| Age continuous<br>Units: years        |         |        |       |
| arithmetic mean                       | 75.9    | 76.2   |       |
| standard deviation                    | ± 8.51  | ± 7.89 | -     |
| Gender categorical<br>Units: Subjects |         |        |       |
| Female                                | 100     | 95     | 195   |
| Male                                  | 75      | 80     | 155   |
| race<br>Units: Subjects               |         |        |       |
| White                                 | 151     | 155    | 306   |
| Black                                 | 22      | 17     | 39    |
| Asian                                 | 1       | 2      | 3     |
| Other                                 | 1       | 1      | 2     |

### Subject analysis sets

|                                                                                                                                                                                                                                                            |                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Subject analysis set title                                                                                                                                                                                                                                 | modified Intent-to-Treat (mITT) |
| Subject analysis set type                                                                                                                                                                                                                                  | Intention-to-treat              |
| Subject analysis set description:<br>All subjects in the safety set (patients that were randomized and received at least one dose of study drug) that had a valid baseline NPI-C A+A assessment and at least one valid post-baseline NPI-C A+A assessment. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                 | Safety Analysis Set             |
| Subject analysis set type                                                                                                                                                                                                                                  | Safety analysis                 |
| Subject analysis set description:<br>All subjects who were enrolled in the study and received at least one dose of study drug were included in safety analyses.                                                                                            |                                 |

| <b>Reporting group values</b> | modified Intent-to-Treat (mITT) | Safety Analysis Set |  |
|-------------------------------|---------------------------------|---------------------|--|
| Number of subjects            | 334                             | 350                 |  |
| Age categorical               |                                 |                     |  |
| Units: Subjects               |                                 |                     |  |
| Adults (18-64 years)          | 30                              | 33                  |  |
| From 65-84 years              | 262                             | 274                 |  |
| 85 years and over             | 42                              | 43                  |  |
| Age continuous                |                                 |                     |  |
| Units: years                  |                                 |                     |  |
| arithmetic mean               |                                 |                     |  |
| standard deviation            | ±                               | ±                   |  |
| Gender categorical            |                                 |                     |  |
| Units: Subjects               |                                 |                     |  |
| Female                        | 187                             | 195                 |  |
| Male                          | 147                             | 155                 |  |
| race                          |                                 |                     |  |
| Units: Subjects               |                                 |                     |  |
| White                         | 290                             | 306                 |  |
| Black                         | 39                              | 39                  |  |
| Asian                         | 3                               | 3                   |  |
| Other                         | 2                               | 2                   |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                            |                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Reporting group title                                                                                                                                                                                                                                      | Placebo                         |
| Reporting group description:<br>Placebo matching ELND005                                                                                                                                                                                                   |                                 |
| Reporting group title                                                                                                                                                                                                                                      | Test                            |
| Reporting group description:<br>ELND005 250 mg                                                                                                                                                                                                             |                                 |
| Subject analysis set title                                                                                                                                                                                                                                 | modified Intent-to-Treat (mITT) |
| Subject analysis set type                                                                                                                                                                                                                                  | Intention-to-treat              |
| Subject analysis set description:<br>All subjects in the safety set (patients that were randomized and received at least one dose of study drug) that had a valid baseline NPI-C A+A assessment and at least one valid post-baseline NPI-C A+A assessment. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                 | Safety Analysis Set             |
| Subject analysis set type                                                                                                                                                                                                                                  | Safety analysis                 |
| Subject analysis set description:<br>All subjects who were enrolled in the study and received at least one dose of study drug were included in safety analyses.                                                                                            |                                 |

### Primary: Change from Baseline in NPI-C A+A Score

|                                                                                                                                |                                         |
|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| End point title                                                                                                                | Change from Baseline in NPI-C A+A Score |
| End point description:<br>Change from Baseline to Week 12 in NPI-C A+A scored between the ELND005 and placebo treatment groups |                                         |
| End point type                                                                                                                 | Primary                                 |
| End point timeframe:<br>12 weeks                                                                                               |                                         |

| End point values                    | Placebo         | Test            |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 155             | 157             |  |  |
| Units: Change from Baseline Score   |                 |                 |  |  |
| least squares mean (standard error) |                 |                 |  |  |
| NPI-C A+A                           | -4.2 (± 0.7)    | -4.3 (± 0.7)    |  |  |

### Statistical analyses

|                                                                                                                        |                                        |
|------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Statistical analysis title                                                                                             | Mixed Model Repeated Measured Analyses |
| Statistical analysis description:<br>Mixed Model Repeated Measured Analyses of Change from Baseline in NPI-C A+A Score |                                        |
| Comparison groups                                                                                                      | Placebo v Test                         |



|                                         |                 |
|-----------------------------------------|-----------------|
| Number of subjects included in analysis | 312             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.8982        |
| Method                                  | t-test, 2-sided |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Mean duration on study for subjects in the ELND005 group was 83.6 days and for subjects in the placebo group was 83.8 days.

Adverse event reporting additional description:

All subjects who were enrolled in the study and received at least one dose of study drug were included in safety analyses.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 17.1   |

### Reporting groups

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

Reporting group description:

All subjects who were randomized into the study and received at least one dose of study drug.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | ELND005 250 mg (Safety) |
|-----------------------|-------------------------|

Reporting group description:

All subjects who were randomized into the study and received at least one dose of study drug.

| Serious adverse events                                              | Placebo Safety  | ELND005 250 mg (Safety) |  |
|---------------------------------------------------------------------|-----------------|-------------------------|--|
| Total subjects affected by serious adverse events                   |                 |                         |  |
| subjects affected / exposed                                         | 5 / 175 (2.86%) | 17 / 175 (9.71%)        |  |
| number of deaths (all causes)                                       | 0               | 0                       |  |
| number of deaths resulting from adverse events                      | 0               | 0                       |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                         |  |
| Colon cancer                                                        |                 |                         |  |
| subjects affected / exposed                                         | 1 / 175 (0.57%) | 0 / 175 (0.00%)         |  |
| occurrences causally related to treatment / all                     | 0 / 5           | 0 / 17                  |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                   |  |
| Rectal cancer                                                       |                 |                         |  |
| subjects affected / exposed                                         | 0 / 175 (0.00%) | 1 / 175 (0.57%)         |  |
| occurrences causally related to treatment / all                     | 0 / 5           | 0 / 17                  |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                   |  |
| Injury, poisoning and procedural complications                      |                 |                         |  |
| Fall                                                                |                 |                         |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 175 (0.57%) | 2 / 175 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acetabulum fracture                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ankle fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hip fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 175 (0.57%) | 0 / 175 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Humerus fracture                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pelvic fracture                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 175 (0.57%) | 0 / 175 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rib fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Cardiac Failure congestive                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 175 (0.57%) | 0 / 175 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Convulsion                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 2 / 175 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cerebellar infarction                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syncope                                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Nausea                                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vomiting                                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Cholelithiasis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal failure acute                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 2 / 175 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary retention                               |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 175 (0.00%) | 2 / 175 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Homocidal ideation                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychotic disorder                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Infections Infestations Sepsis                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 3 / 175 (1.71%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary Tract Infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 3 / 175 (1.71%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection enterococcal            |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Type 2 diabetes mellitus                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 175 (0.00%) | 1 / 175 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 17          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                                                    | Placebo Safety    | ELND005 250 mg<br>(Safety) |  |
|--------------------------------------------------------------------------------------|-------------------|----------------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 82 / 175 (46.86%) | 97 / 175 (55.43%)          |  |
| Injury, poisoning and procedural complications                                       |                   |                            |  |
| Fall                                                                                 |                   |                            |  |
| subjects affected / exposed                                                          | 9 / 175 (5.14%)   | 11 / 175 (6.29%)           |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Contusion                                                                            |                   |                            |  |
| subjects affected / exposed                                                          | 7 / 175 (4.00%)   | 1 / 175 (0.57%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Nervous system disorders                                                             |                   |                            |  |
| Dizziness                                                                            |                   |                            |  |
| subjects affected / exposed                                                          | 7 / 175 (4.00%)   | 2 / 175 (1.14%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Lethargy                                                                             |                   |                            |  |
| subjects affected / exposed                                                          | 2 / 175 (1.14%)   | 6 / 175 (3.43%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Somnolence                                                                           |                   |                            |  |
| subjects affected / exposed                                                          | 4 / 175 (2.29%)   | 3 / 175 (1.71%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Headache                                                                             |                   |                            |  |
| subjects affected / exposed                                                          | 2 / 175 (1.14%)   | 4 / 175 (2.29%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| General disorders and administration site conditions                                 |                   |                            |  |
| Gait disturbance                                                                     |                   |                            |  |
| subjects affected / exposed                                                          | 1 / 175 (0.57%)   | 4 / 175 (2.29%)            |  |
| occurrences (all)                                                                    | 82                | 97                         |  |
| Gastrointestinal disorders                                                           |                   |                            |  |
| Diarrhoea                                                                            |                   |                            |  |

|                                                                                                              |                        |                        |  |
|--------------------------------------------------------------------------------------------------------------|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                             | 5 / 175 (2.86%)<br>82  | 14 / 175 (8.00%)<br>97 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                 | 5 / 175 (2.86%)<br>82  | 5 / 175 (2.86%)<br>97  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                             | 2 / 175 (1.14%)<br>82  | 4 / 175 (2.29%)<br>97  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 2 / 175 (1.14%)<br>82  | 7 / 175 (4.00%)<br>97  |  |
| Psychiatric disorders<br>Agitation<br>subjects affected / exposed<br>occurrences (all)                       | 13 / 175 (7.43%)<br>82 | 14 / 175 (8.00%)<br>97 |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                                 | 7 / 175 (4.00%)<br>82  | 5 / 175 (2.86%)<br>97  |  |
| Infections and infestations<br>Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)   | 7 / 175 (4.00%)<br>82  | 12 / 175 (6.86%)<br>97 |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                                               | 5 / 175 (2.86%)<br>82  | 2 / 175 (1.14%)<br>97  |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 4 / 175 (2.29%)<br>82  | 3 / 175 (1.71%)<br>97  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported