



## Clinical trial results: A Prospective Study of the Clinical Outcome Following Treatment Discontinuation After Remission in First-Episode Schizophrenia Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001221-16 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 11 March 2010  |

### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 15 July 2016   |
| First version publication date | 09 August 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Review of data</li></ul> |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | RISSCH3024 |
|-----------------------|------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00378092 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Janssen-Cilag Medical Affairs EMEA  |
| Sponsor organisation address | Turnhoutseweg 30, B-2340 Beerse, Belgium,   |
| Public contact               | Janssen Research and Development, Clinical Registry Group-JB BV, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Janssen Research and Development, Clinical Registry Group-JB BV, ClinicalTrialsEU@its.jnj.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? | Yes |

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 11 March 2010 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 11 March 2010 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the time to relapse after discontinuation of RLAI (Risperidone Long Acting Injection) in first- episode subjects successfully treated for 2 years with RLAI. The relapse rate after treatment discontinuation, the time to response after re-exposure to treatment with RLAI and the degree of clinical improvement measured by PANSS were also evaluated.

Protection of trial subjects:

Safety was evaluated based on analysis of adverse events, clinical laboratory tests (hematology, serum chemistry, prolactin), vital sign measurements, electrocardiogram (ECGs), physical examinations, extrapyramidal symptoms (EPS), body weight and body mass index (BMI), and waist/hip circumference.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 25 April 2006 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | South Africa: 33 |
| Worldwide total number of subjects   | 33               |
| EEA total number of subjects         | 0                |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 1  |
| Adults (18-64 years)                      | 32 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 33 subjects entered Period 1 and discontinued their existing antipsychotic treatment. None of the subjects completed the 36-month follow-up period. A total of 31 subjects entered Period 2 and restarted Risperidone Long-Acting Injection (RLAI) treatment. Overall, 14 of the 31 subjects in Period 2 completed the 24 month treatment period.

### Pre-assignment

Screening details:

In Period 1, existing RLAI treatment was discontinued. Subjects who experienced a relapse during Period 1 were transferred into Period 2, at which time RLAI and oral risperidone treatment was initiated simultaneously. Risperidone LAI was initiated at a dose of 25 milligram (mg) once every 2 weeks and continued for a maximum of 2 years in Period 2.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Discontinuation             |
| Is this the baseline period? | Yes                         |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

### Arms

|           |                      |
|-----------|----------------------|
| Arm title | Risperidone Period 1 |
|-----------|----------------------|

Arm description:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Risperidone                                     |
| Investigational medicinal product code |   |
| Other name                             | Risperidal                                      |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

|                                       |                      |
|---------------------------------------|----------------------|
| <b>Number of subjects in period 1</b> | Risperidone Period 1 |
| Started                               | 33                   |
| Completed                             | 32                   |
| Not completed                         | 1                    |
| Lost to follow-up                     | 1                    |

## Period 2

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | After Relapse               |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

## Arms

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | Risperidone Period 2 |
|------------------|----------------------|

Arm description:

In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Risperidone                                     |
| Investigational medicinal product code |   |
| Other name                             | Risperidal                                      |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Risperidone Period 2 |
|---|----------------------|
| Started   | 31                   |
| Completed   | 14                   |
| Not completed                                       | 17                   |
| Consent withdrawn by subject                        | 2                    |
| Adverse event, non-fatal                            | 1                    |
| Other   | 6                    |
| Lost to follow-up                                   | 5                    |
| Lack of efficacy                                    | 3                    |

Notes:

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

Justification: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period

## Baseline characteristics

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Risperidone Period 1 |
|-----------------------|----------------------|

Reporting group description:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

| Reporting group values                      | Risperidone Period 1 | Total |  |
|---|----------------------|-------|--|
| Number of subjects                          | 33                   | 33    |  |
| Title for AgeCategorical<br>Units: subjects |                      |       |  |
| Children (2-11 years)                       | 0                    | 0     |  |
| Adolescents (12-17 years)                   | 1                    | 1     |  |
| Adults (18-64 years)                        | 32                   | 32    |  |
| From 65 to 84 years                         | 0                    | 0     |  |
| 85 years and over                           | 0                    | 0     |  |
| Title for AgeContinuous<br>Units: years     |                      |       |  |
| arithmetic mean                             | 27.5                 |       |  |
| standard deviation                          | ± 7.92               | -     |  |
| Title for Gender<br>Units: subjects         |                      |       |  |
| Female                                      | 14                   | 14    |  |
| Male  | 19                   | 19    |  |

## End points

### End points reporting groups

|   |                      |
|---|----------------------|
| Reporting group title   | Risperidone Period 1 |
| Reporting group description:  |                      |
| In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.     |                      |
| Reporting group title   | Risperidone Period 2 |
| Reporting group description:  |                      |
| In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks. |                      |

### Primary: Time to Relapse After Discontinuation of Risperidone Long-Acting Injection (RLAI) in First-Episode Subjects Successfully Treated for 24 Months With RLAI in Previous Study (RIS-PSY-301) (Period 1)

|                 |  |
|-----------------|--|
| End point title | Time to Relapse After Discontinuation of Risperidone Long-Acting Injection (RLAI) in First-Episode Subjects Successfully Treated for 24 Months With RLAI in Previous Study (RIS-PSY-301) (Period 1) <sup>[1]</sup> |
|-----------------|--|

#### End point description:

Relapse was diagnosed if 1 or more of the following occurred: a 25 percent increase in Positive and Negative Syndrome Scale (PANSS) total score ranging from 30 (absent) to 210 (extreme ill); Clinical Global Impression (CGI-C) score of 6 ('much worse'); deliberate self-injury; emergence of clinically significant suicidal or homicidal ideation; or violent behavior resulting in significant injury to another person or significant property damage (as per Adverse Event reporting). The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

#### End point timeframe:

Month 36 or early withdrawal (EW)

#### 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: No statistical analysis were performed for this endpoint

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Risperidone Period 1 |  |  |  |
| Subject group type            | Reporting group      |  |  |  |
| Number of subjects analysed   | 32 <sup>[2]</sup>    |  |  |  |
| Units: units on a scale       |                      |  |  |  |
| median (full range (min-max)) | 154 (34 to 880)      |  |  |  |

#### Notes:

[2] - Here 'N' signifies number of subjects analysed for this endpoint.

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects who Relapsed After Discontinuation of RLAI (Period 1)

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects who Relapsed After Discontinuation of RLAI (Period 1) <sup>[3]</sup> |
|-----------------|---|

#### End point description:

Relapse was diagnosed if 1 or more of the following occurred: a 25 percent increase in PANSS total score

ranging from 30 (absent) to 210 (extreme ill); CGI-C score of 6 ('much worse'); deliberate self-injury; emergence of clinically significant suicidal or homicidal ideation; or violent behavior resulting in significant injury to another person or significant property damage (as per Adverse Event reporting). The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Month 36 or EW

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: No statistical analysis were performed for this endpoint

|                               |                      |  |  |  |
|-------------------------------|----------------------|--|--|--|
| <b>End point values</b>       | Risperidone Period 1 |  |  |  |
| Subject group type            | Reporting group      |  |  |  |
| Number of subjects analysed   | 32 <sup>[4]</sup>    |  |  |  |
| Units: percentage of subjects |                      |  |  |  |
| number (not applicable)       | 97                   |  |  |  |

Notes:

[4] - Here 'N' signifies number of subjects analysed for this endpoint.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score After Re-Initiation of RLAI, at Month 24 or Early Withdrawal (EW)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score After Re-Initiation of RLAI, at Month 24 or Early Withdrawal (EW) <sup>[5]</sup> |
|-----------------|---|

End point description:

The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

Notes:

[5] - 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: No statistical analysis were performed for this endpoint

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | Risperidone Period 2 |  |  |  |
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 31                   |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Baseline (n=31)                      | 86.5 (± 14.4)        |  |  |  |
| Month 24 (n=30)                      | -27.7 (± 20.6)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Time to Treatment Response After Re-Initiation of RLAI (Period 2)

|                 |  |
|-----------------|--|
| End point title | Time to Treatment Response After Re-Initiation of RLAI (Period 2) <sup>[6]</sup> |
|-----------------|--|

End point description:

Time to treatment response after re-initiation of RLAI was the time that elapse between baseline assessment of PANSS for Period 2 and fulfillment of the response which is defined as greater than or equal to 20 percent improvement in PANSS total score. PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Month 24 or EW

Notes:

[6] - 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: No statistical analysis were performed for this endpoint

| End point values                 | Risperidone<br>Period 2 |  |  |  |
|----------------------------------|-------------------------|--|--|--|
| Subject group type               | Reporting group         |  |  |  |
| Number of subjects analysed      | 31                      |  |  |  |
| Units: days                      |                         |  |  |  |
| median (confidence interval 95%) |                         |  |  |  |
| Time to 20% Response             | 39 (27 to 43)           |  |  |  |
| Time to 30% Response             | 41 (29 to 44)           |  |  |  |
| Time to 40% Response             | 43 (41 to 56)           |  |  |  |
| Time to 50% Response             | 83 (44 to 112)          |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|--|

End point description:

The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology (GP) subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all



subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

|                             |           |
|-----------------------------|-----------|
| End point type              | Secondary |
| End point timeframe:        |           |
| Baseline and Month 36 or EW |           |

| End point values                      | Risperidone<br>Period 1 |  |  |  |
|---------------------------------------|-------------------------|--|--|--|
| Subject group type                    | Reporting group         |  |  |  |
| Number of subjects analysed           | 33                      |  |  |  |
| Units: units on a scale               |                         |  |  |  |
| arithmetic mean (standard deviation)  |                         |  |  |  |
| Baseline: Positive subscale           | 7.3 (± 1.2)             |  |  |  |
| Change at Month 36: Positive subscale | 13.4 (± 5.4)            |  |  |  |
| Baseline: Negative subscale           | 16.1 (± 4.7)            |  |  |  |
| Change at Month 36: Negative subscale | 8.2 (± 6)               |  |  |  |
| Baseline: GP subscale                 | 21.4 (± 3.4)            |  |  |  |
| Change at Month 36: GP subscale       | 20.2 (± 8.6)            |  |  |  |
| Baseline: Total score                 | 44.8 (± 7.4)            |  |  |  |
| Change at Month 36: Total score       | 41.8 (± 15)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 24 or Early Withdrawal (EW) (Period 2)

|  |  |
|--|--|
| End point title  | Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 24 or Early Withdrawal (EW) (Period 2) |
| End point description:   |  |
| <p>The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology (GP) subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.</p> |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline and Month 24 or EW  |  |

| End point values                     | Risperidone<br>Period 2 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 31                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline: Positive subscale (n=31)   | 20.6 (± 3.9)            |  |  |  |

|  |                |  |  |  |
|--|----------------|--|--|--|
| Change at Month 24: Positive subscale (n=30) | -8.8 (± 7.1)   |  |  |  |
| Baseline: Negative subscale (n=31)           | 23.9 (± 6.3)   |  |  |  |
| Change at Month 24: Negative subscale (n=30) | -4.7 (± 4.9)   |  |  |  |
| Baseline: GP subscale (n=31)                 | 41.9 (± 8)     |  |  |  |
| Change at Month 24: GP subscale (n=30)       | -14.2 (± 10.8) |  |  |  |
| Baseline: Total score (n=31)                 | 86.5 (± 14.4)  |  |  |  |
| Change at Month 24: Total score (n=30)       | -50.8 (± 35)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Marder PANSS Subscales Score at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Marder PANSS Subscales Score at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|--|

End point description:

The PANSS total score consists of the sum of all 30 PANSS items and score ranges from 30 to 210. Higher scores indicate worsening. The symptoms are rated on a 7-point Marder scale from 1 (absent) to 7 (extreme psychopathology). Positive symptoms subscale consists of 8 items with total score range of 8-56; negative symptoms subscale and disorganized thoughts subscale, each consists of 7 items with total score range of 7-49, uncontrolled hostility (UH) or excitement subscale and anxiety/depression subscale, each consists of 4 items with total score range of 4-28. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 36 or EW

| End point values                             | Risperidone<br>Period 1 |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                           | Reporting group         |  |  |  |
| Number of subjects analysed                  | 33                      |  |  |  |
| Units: units on a scale                      |                         |  |  |  |
| arithmetic mean (standard deviation)         |                         |  |  |  |
| Baseline: Positive symptoms factor           | 11.6 (± 2.4)            |  |  |  |
| Change at Month 24: Positive symptoms factor | 15.5 (± 5.2)            |  |  |  |
| Baseline: Negative symptoms factor           | 13.2 (± 4.6)            |  |  |  |
| Change at Month 24: Negative symptoms factor | 7.5 (± 6.9)             |  |  |  |
| Baseline: Disorganised thoughts              | 11.8 (± 2)              |  |  |  |
| Change at Month 24: Disorganised thoughts    | 9.9 (± 4)               |  |  |  |
| Baseline: Uncontrolled hostility             | 4.1 (± 0.2)             |  |  |  |
| Change at Month 24: Uncontrolled hostility   | 4.5 (± 4.3)             |  |  |  |
| Baseline: Anxiety/depression                 | 4.1 (± 0.7)             |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| Change at Month 24:<br>Anxiety/depression | 4.4 ( $\pm$ 3) |  |  |  |
|---|----------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Marder PANSS Subscales Score at Month 24 or Early Withdrawal (EW) (Period 2)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Marder PANSS Subscales Score at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|--|

End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The symptoms are rated on a 7-point Marder scale from 1 (absent) to 7 (extreme psychopathology). Positive symptoms subscale consists of 8 items with total score range of 8-56; negative symptoms subscale and disorganized thoughts subscale, each consists of 7 items with total score range of 7-49, UH or excitement subscale and anxiety or depression subscale, each consists of 4 items with total score range of 4-28. Higher score indicates greater severity. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

| End point values                                   | Risperidone<br>Period 2 |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                                 | Reporting group         |  |  |  |
| Number of subjects analysed                        | 31                      |  |  |  |
| Units: units on a scale                            |                         |  |  |  |
| arithmetic mean (standard deviation)               |                         |  |  |  |
| Baseline: Positive symptoms factor (n=31)          | 27.2 ( $\pm$ 4.4)       |  |  |  |
| Change at Month 24: Positive symptoms factor(n=30) | -9.8 ( $\pm$ 7.8)       |  |  |  |
| Baseline: Negative symptoms factor (n=31)          | 20.6 ( $\pm$ 7.1)       |  |  |  |
| Change at Month 24:Negative Symptoms factor (n=30) | -5.8 ( $\pm$ 5.5)       |  |  |  |
| Baseline: Disorganised Thoughts (n=31)             | 21.7 ( $\pm$ 4.2)       |  |  |  |
| Change at Month 24: Disorganised Thoughts (n=30)   | -5.7 ( $\pm$ 5.9)       |  |  |  |
| Baseline: Uncontrolled Hostility (n=31)            | 8.2 ( $\pm$ 3.6)        |  |  |  |
| Change at Month 24: Uncontrolled Hostility (n=30)  | -2.5 ( $\pm$ 5.2)       |  |  |  |
| Baseline: Anxiety/Depression (n=31)                | 8.7 ( $\pm$ 2.9)        |  |  |  |
| Change at Month 24: Anxiety/Depression (n=30)      | -3.9 ( $\pm$ 3)         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Disease Remission Based on PANSS (Period 1)

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Disease Remission Based on PANSS (Period 1) |
|-----------------|---|

End point description:

A subject was 'in remission' when he/she was symptomatically stable and showed progressive improvement in total recovery according to severity (mild or less simultaneously on 8 PANSS items: P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, G9 unusual thought content, G5 mannerisms and posturing, N1 blunted affect, N4 social withdrawal, N6 lack of spontaneity or flow of conversation) and time (scores for 8 PANSS items above did not exceed the severity criterion mild at any time point of assessment for at least 6 months to meet the criteria of remission) criteria. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Month 36 or EW

| End point values            | Risperidone<br>Period 1 |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 33                      |  |  |  |
| Units: subjects             |                         |  |  |  |
| Baseline                    | 28                      |  |  |  |
| Month 36                    | 1                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Disease Remission Based on PANSS (Period 2)

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Disease Remission Based on PANSS (Period 2) |
|-----------------|---|

End point description:

A subject was 'in remission' when he/she was symptomatically stable and showed progressive improvement in total recovery according to severity (mild or less simultaneously on 8 PANSS items: P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, G9 unusual thought content, G5 mannerisms and posturing, N1 blunted affect, N4 social withdrawal, N6 lack of spontaneity or flow of conversation) and time (scores for 8 PANSS items above did not exceed the severity criterion mild at any time point of assessment for at least 6 months to meet the criteria of remission) criteria. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment. Disease Remission Based on PANSS was not seen till the end of period 2 (Month 24).

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

End point timeframe:

Early Withdrawal (Period 2)

|                             |                         |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| <b>End point values</b>     | Risperidone<br>Period 2 |  |  |  |
| Subject group type          | Reporting group         |  |  |  |
| Number of subjects analysed | 31                      |  |  |  |
| Units: subjects             | 14                      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

|  |  |
|--|--|
| End point title  | Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1) |
| End point description:<br>The CGI-S scale is a 7-point global assessment that measures the Clinician's impression of the severity of illness exhibited by a subject. A rating of '1=Normal, not at all ill' and a rating of '7=Among the most extremely ill subjects'. Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline and Month 36 or EW  |  |

|                                      |                         |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| <b>End point values</b>              | Risperidone<br>Period 1 |  |  |  |
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 33                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=33)                      | 1.3 (± 0.6)             |  |  |  |
| Change at Month 36 (n=33)            | 2.7 (± 1.1)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

|  |  |
|--|--|
| End point title  | Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2) |
| End point description:<br>The CGI-S scale is a 7-point global assessment that measures the Clinician's impression of the severity of illness exhibited by a subject. A rating of '1=Normal, not at all ill' and a rating of '7=Among the most extremely ill subjects'. Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment. |  |
| End point type   | Secondary  |

End point timeframe:

Baseline and Month 24 or EW

| End point values                     | Risperidone<br>Period 2 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 31                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=31)                      | 4 ( $\pm$ 0.7)          |  |  |  |
| Change at Month 24 (n=30)            | -1.9 ( $\pm$ 1.6)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|---|

End point description:

The CDSS assesses the level of depression in subjects with schizophrenia. It consists of 9 items: depression, hopelessness, self-depreciation, pathological guilt, guilty ideas of reference, morning depression, early awakening, suicidal, observed depression, each scored on a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe). The total score is a sum of the scores of each item and may range from 0 to 27. Higher score indicates more severe pathology. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 36 or EW

| End point values                     | Risperidone<br>Period 1 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 33                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=33)                      | 0.4 ( $\pm$ 1.9)        |  |  |  |
| Change at Month 36 (n=33)            | 1.8 ( $\pm$ 3.8)        |  |  |  |

### Statistical analyses

No statistical analyses for this end point

---

**Secondary: Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 24 or Early Withdrawal (EW) (Period 2)**

---

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|---|

End point description:

The CDSS assesses the level of depression in subjects with schizophrenia. It consists of 9 items: depression, hopelessness, self depreciation, pathological guilt, guilty ideas of reference, morning depression, early awakening, suicidal, observed depression, each scored on a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe). The total score is a sum of the scores of each item and may range from 0 to 27. Higher score indicates more severe pathology. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

---

| End point values                     | Risperidone<br>Period 2 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 31                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=31)                      | 2.4 (± 3.2)             |  |  |  |
| Change at Month 24 (n=30)            | -2.2 (± 3.4)            |  |  |  |

---

**Statistical analyses**

---

No statistical analyses for this end point

---

**Secondary: Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 36 or Early Withdrawal (EW) (Period 1)**

---

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|--|

End point description:

The SOFAS is a 100-point single item scale that assesses level of social and occupational functioning of a subject and is not directly influenced by the overall severity of the individual's psychological symptoms. The scale values range from 1=most impaired to 100=healthiest individual. The scale also included a rating point of 0=missing information. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 36 or EW

---

|                                      |                         |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| <b>End point values</b>              | Risperidone<br>Period 1 |  |  |  |
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 33                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=33)                      | 66.4 (± 4.7)            |  |  |  |
| Change at Month 36 or EW (n=33)      | -25 (± 10.6)            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 24 or Early Withdrawal (EW) (Period 2)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|--|

End point description:

The SOFAS is a 100-point single item scale that assesses level of social and occupational functioning of a subject and is not directly influenced by the overall severity of the individual's psychological symptoms. The scale values range from 1=most impaired to 100=healthiest individual. The scale also included a rating point of 0=missing information. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

|                                      |                         |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| <b>End point values</b>              | Risperidone<br>Period 2 |  |  |  |
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 31                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=31)                      | 41.5 (± 8)              |  |  |  |
| Change at Month 24 (n=30)            | 14.7 (± 14.7)           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Baseline (n=33)Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |   |
|-----------------|---|
| End point title | Baseline (n=33)Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|---|



End point description:

The PGI-S is an 11-point (0=very well to 10=very poor) scale that requires the subjects to rate the severity of their illness at the time of assessment, relative to the subject's past experience. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 36 or EW

| End point values                     | Risperidone<br>Period 1 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 33                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=33)                      | 1.2 (± 0.5)             |  |  |  |
| Change at Month 36 or EW (n=33)      | 1.3 (± 1.2)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patient Global Impression-Change (PGI-C) Score at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |  |
|-----------------|--|
| End point title | Patient Global Impression-Change (PGI-C) Score at Month 36 or Early Withdrawal (EW) (Period 1) |
|-----------------|--|

End point description:

The PGI-C is a 7-point scale that requires the subjects to assess how much their illness has improved or worsened relative to a baseline state at the beginning of the intervention. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Month 36 or EW

| End point values                     | Risperidone<br>Period 1 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 33                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=33)                      | 1.2 (± 0.5)             |  |  |  |
| Change at Month 36 or EW (n=32)      | 1.3 (± 1.2)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|--|

End point description:

The PGI-S is an 11-point (0=very well to 10=very poor) scale that requires the subjects to rate the severity of their illness at the time of assessment, relative to the subject's past experience. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

| End point values                     | Risperidone<br>Period 2 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 30 <sup>[7]</sup>       |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=30)                      | 2.7 (± 1.3)             |  |  |  |
| Change at Month 24 (n=29)            | -1 (± 1.8)              |  |  |  |

Notes:

[7] - Here 'N' signifies number of subjects analysed for this endpoint.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Patient Global Impression-Change (PGI-C) Score at Month 24 or Early Withdrawal (EW) (Period 2)

|                 |  |
|-----------------|--|
| End point title | Patient Global Impression-Change (PGI-C) Score at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|--|

End point description:

The PGI-C is a 7-point scale that requires the subjects to assess how much their illness has improved or worsened relative to a baseline state at the beginning of the intervention. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Month 24 or EW

| End point values                     | Risperidone<br>Period 2 |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 31                      |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline (n=31)                      | 2.7 (± 1.3)             |  |  |  |
| Month 24 (n=30)                      | 2.6 (± 1)               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in 12-Item Short-Form (SF-12) Score -Quality of Life Survey at Month 36 or Early Withdrawal (EW) (Period 1)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in 12-Item Short-Form (SF-12) Score -<br>Quality of Life Survey at Month 36 or Early Withdrawal (EW)<br>(Period 1) |
|-----------------|---|

End point description:

The SF-12 is a validated 12 question quality-of-life questionnaire. The SF-12 extracts 12 items from the SF-36 questionnaire in 2 six-item subscales: physical component summary (PCS) and MCS (mental component summary). The SF-12 score ranges from 10=maximum impairment to 70=no impairment. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 36 or EW

| End point values                                   | Risperidone<br>Period 1 |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                                 | Reporting group         |  |  |  |
| Number of subjects analysed                        | 33                      |  |  |  |
| Units: units on a scale                            |                         |  |  |  |
| arithmetic mean (standard deviation)               |                         |  |  |  |
| Physical component, Baseline (n=33)                | 52 (± 6.2)              |  |  |  |
| Physical Component: change at M 36 or<br>EW (N=32) | -6.1 (± 10.7)           |  |  |  |
| Mental Component, Baseline (n=33)                  | 48.3 (± 10.8)           |  |  |  |
| Mental Component: change at M 36 or<br>EW (n=32)   | -7.2 (± 12.7)           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in 12-Item Short-Form (SF-12) Score - Quality of Life Survey at Month 24 or Early Withdrawal (EW) (Period 2)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in 12-Item Short-Form (SF-12) Score - Quality of Life Survey at Month 24 or Early Withdrawal (EW) (Period 2) |
|-----------------|---|

End point description:

The SF-12 is a validated 12 question quality-of-life questionnaire. The SF-12 extracts 12 items from the SF-36 questionnaire in 2 six-item subscales: physical component summary (PCS) and MCS (mental component summary). The SF-12 scores range from 10=maximum impairment to 70=no impairment. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

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

End point timeframe:

Baseline and Month 24 or EW

| End point values                         | Risperidone<br>Period 2 |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                       | Reporting group         |  |  |  |
| Number of subjects analysed              | 30 <sup>[8]</sup>       |  |  |  |
| Units: units on a scale                  |                         |  |  |  |
| arithmetic mean (standard deviation)     |                         |  |  |  |
| Physical Component, Baseline (n=30)      | 45.1 (± 9.8)            |  |  |  |
| Physical Component, Change at M24 (n=29) | 2.6 (± 12.3)            |  |  |  |
| Mental Component, Baseline (n=30)        | 40.8 (± 10.7)           |  |  |  |
| Mental Component, Change at M 24 (n=29)  | 5.8 (± 12.1)            |  |  |  |

Notes:

[8] - Here 'N' signifies number of subjects analysed for this endpoint.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Month 36 (Period 1) or Month 24 (Period 24)

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 9.0 |
|--------------------|-----|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Risperidone PERIOD 2 |
|-----------------------|----------------------|

Reporting group description:

In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Risperidone PERIOD 1 |
|-----------------------|----------------------|

Reporting group description:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

| Serious adverse events                            | Risperidone PERIOD 2 | Risperidone PERIOD 1 |  |
|---|----------------------|----------------------|--|
| Total subjects affected by serious adverse events |                      |                      |  |
| subjects affected / exposed                       | 9 / 31 (29.03%)      | 5 / 33 (15.15%)      |  |
| number of deaths (all causes)                     | 0                    | 0                    |  |
| number of deaths resulting from adverse events    |                      |                      |  |
| Injury, poisoning and procedural complications    |                      |                      |  |
| Road Traffic Accident                             |                      |                      |  |
| subjects affected / exposed                       | 1 / 31 (3.23%)       | 0 / 33 (0.00%)       |  |
| occurrences causally related to treatment / all   | 0 / 1                | 0 / 0                |  |
| deaths causally related to treatment / all        | 0 / 0                | 0 / 0                |  |
| Psychiatric disorders                             |                      |                      |  |
| Suicidal Ideation                                 |                      |                      |  |
| subjects affected / exposed                       | 1 / 31 (3.23%)       | 0 / 33 (0.00%)       |  |
| occurrences causally related to treatment / all   | 0 / 1                | 0 / 0                |  |
| deaths causally related to treatment / all        | 0 / 0                | 0 / 0                |  |
| Psychotic Disorder                                |                      |                      |  |
| subjects affected / exposed                       | 6 / 31 (19.35%)      | 5 / 33 (15.15%)      |  |
| occurrences causally related to treatment / all   | 0 / 8                | 0 / 5                |  |
| deaths causally related to treatment / all        | 0 / 0                | 0 / 0                |  |
| Metabolism and nutrition disorders                |                      |                      |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Diabetes Mellitus                               |                |                |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) | 0 / 33 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Risperidone PERIOD<br>2 | Risperidone PERIOD<br>1 |  |
|---|-------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                         |                         |  |
| subjects affected / exposed                           | 22 / 31 (70.97%)        | 33 / 33 (100.00%)       |  |
| Investigations  |                         |                         |  |
| Blood Creatine Phosphokinase Increased                |                         |                         |  |
| subjects affected / exposed                           | 2 / 31 (6.45%)          | 0 / 33 (0.00%)          |  |
| occurrences (all)                                     | 2                       | 0                       |  |
| Blood Cholesterol Increased                           |                         |                         |  |
| subjects affected / exposed                           | 0 / 31 (0.00%)          | 4 / 33 (12.12%)         |  |
| occurrences (all)                                     | 0                       | 4                       |  |
| Blood Glucose Increased                               |                         |                         |  |
| subjects affected / exposed                           | 0 / 31 (0.00%)          | 2 / 33 (6.06%)          |  |
| occurrences (all)                                     | 0                       | 2                       |  |
| Blood Prolactin Increased                             |                         |                         |  |
| subjects affected / exposed                           | 6 / 31 (19.35%)         | 2 / 33 (6.06%)          |  |
| occurrences (all)                                     | 6                       | 2                       |  |
| Weight Increased                                      |                         |                         |  |
| subjects affected / exposed                           | 8 / 31 (25.81%)         | 0 / 33 (0.00%)          |  |
| occurrences (all)                                     | 8                       | 0                       |  |
| Blood Triglycerides Increased                         |                         |                         |  |
| subjects affected / exposed                           | 3 / 31 (9.68%)          | 1 / 33 (3.03%)          |  |
| occurrences (all)                                     | 3                       | 1                       |  |
| Gamma-Glutamyltransferase Increased                   |                         |                         |  |
| subjects affected / exposed                           | 0 / 31 (0.00%)          | 2 / 33 (6.06%)          |  |
| occurrences (all)                                     | 0                       | 2                       |  |
| Weight Decreased                                      |                         |                         |  |
| subjects affected / exposed                           | 2 / 31 (6.45%)          | 6 / 33 (18.18%)         |  |
| occurrences (all)                                     | 2                       | 6                       |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| Vascular disorders                       |                 |                |  |
| Hypertension                             |                 |                |  |
| subjects affected / exposed              | 2 / 31 (6.45%)  | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 2               | 0              |  |
| Nervous system disorders                 |                 |                |  |
| Headache                                 |                 |                |  |
| subjects affected / exposed              | 5 / 31 (16.13%) | 2 / 33 (6.06%) |  |
| occurrences (all)                        | 5               | 2              |  |
| Parkinsonism                             |                 |                |  |
| subjects affected / exposed              | 3 / 31 (9.68%)  | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 3               | 0              |  |
| Sedation                                 |                 |                |  |
| subjects affected / exposed              | 2 / 31 (6.45%)  | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 3               | 0              |  |
| Tremor                                   |                 |                |  |
| subjects affected / exposed              | 2 / 31 (6.45%)  | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 2               | 0              |  |
| Gastrointestinal disorders               |                 |                |  |
| Diarrhoea                                |                 |                |  |
| subjects affected / exposed              | 4 / 31 (12.90%) | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 4               | 0              |  |
| Nausea                                   |                 |                |  |
| subjects affected / exposed              | 4 / 31 (12.90%) | 1 / 33 (3.03%) |  |
| occurrences (all)                        | 5               | 1              |  |
| Toothache                                |                 |                |  |
| subjects affected / exposed              | 3 / 31 (9.68%)  | 1 / 33 (3.03%) |  |
| occurrences (all)                        | 4               | 1              |  |
| Vomiting                                 |                 |                |  |
| subjects affected / exposed              | 2 / 31 (6.45%)  | 0 / 33 (0.00%) |  |
| occurrences (all)                        | 3               | 0              |  |
| Reproductive system and breast disorders |                 |                |  |
| Menorrhagia                              |                 |                |  |
| subjects affected / exposed              | 0 / 31 (0.00%)  | 2 / 33 (6.06%) |  |
| occurrences (all)                        | 0               | 2              |  |
| Psychiatric disorders                    |                 |                |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| Depression                                      |                 |                  |  |
| subjects affected / exposed                     | 3 / 31 (9.68%)  | 1 / 33 (3.03%)   |  |
| occurrences (all)                               | 5               | 1                |  |
| Anxiety   |                 |                  |  |
| subjects affected / exposed                     | 2 / 31 (6.45%)  | 1 / 33 (3.03%)   |  |
| occurrences (all)                               | 2               | 1                |  |
| Insomnia  |                 |                  |  |
| subjects affected / exposed                     | 6 / 31 (19.35%) | 7 / 33 (21.21%)  |  |
| occurrences (all)                               | 13              | 9                |  |
| Psychotic Disorder                              |                 |                  |  |
| subjects affected / exposed                     | 8 / 31 (25.81%) | 29 / 33 (87.88%) |  |
| occurrences (all)                               | 13              | 29               |  |
| Restlessness                                    |                 |                  |  |
| subjects affected / exposed                     | 7 / 31 (22.58%) | 8 / 33 (24.24%)  |  |
| occurrences (all)                               | 8               | 8                |  |
| Musculoskeletal and connective tissue disorders |                 |                  |  |
| Back Pain                                       |                 |                  |  |
| subjects affected / exposed                     | 2 / 31 (6.45%)  | 0 / 33 (0.00%)   |  |
| occurrences (all)                               | 2               | 0                |  |
| Musculoskeletal Stiffness                       |                 |                  |  |
| subjects affected / exposed                     | 3 / 31 (9.68%)  | 0 / 33 (0.00%)   |  |
| occurrences (all)                               | 4               | 0                |  |
| Infections and infestations                     |                 |                  |  |
| Influenza                                       |                 |                  |  |
| subjects affected / exposed                     | 4 / 31 (12.90%) | 0 / 33 (0.00%)   |  |
| occurrences (all)                               | 5               | 0                |  |
| Nasopharyngitis                                 |                 |                  |  |
| subjects affected / exposed                     | 3 / 31 (9.68%)  | 0 / 33 (0.00%)   |  |
| occurrences (all)                               | 5               | 0                |  |



## **More information**

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

Were there any global substantial amendments to the protocol? No

---

### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported