



## Clinical trial results:

### Efficacy and learning skill after OROS Methylphenidate treatment in adolescents with Attention-Deficit/Hyperactivity Disorder: A 12-week, multi-center, open-label study

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001084-39 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 23 April 2010  |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 01 July 2016   |
| First version publication date | 13 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 | CONCERTAATT4082 |
|-----------------------|-----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01060150 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Janssen Research and Development  |
| Sponsor organisation address | Archimedesweg 29, Leiden, Netherlands, 2333CM   |
| Public contact               | Clinical Registry Group-JB BV, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group-JB BV, Janssen Research and Development, 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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 23 April 2010 |
| Is this the analysis of the primary completion data? | No            |

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|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 23 April 2010 |
| Was the trial ended prematurely? | No            |

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Notes:

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**General information about the trial**

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Main objective of the trial:

The primary objective of this study was to identify efficacy of 12-week treatment of open-Labeled Osmotic Release Oral System (OROS) methylphenidate by changes of K-ADHD Rating Scale (K-ARS) and Clinical Global Impression – Severity (CGI) scores in Korean Attention Deficit Hyperactivity Disorder (ADHD) adolescents and to evaluate by changes of Learning Skill Test (LST) scores whether there was a change in learning skill in adolescents affected by drug treatment.

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Protection of trial subjects:

Safety evaluations for this study included the monitoring of adverse events, clinical laboratory tests (hematology, serum chemistry and urinalysis), vital sign measurements, physical examination and electrocardiogram (EKG).

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Background therapy: -

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Evidence for comparator: -

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|   |              |
|---|--------------|
| Actual start date of recruitment                          | 27 June 2008 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 113 |
| Worldwide total number of subjects   | 113                     |
| EEA total number of subjects         | 0                       |

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Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                 | 104 |
| Adults (18-64 years)                      | 9   |
| From 65 to 84 years                       | 0   |

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|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

A total of 115 subjects were enrolled in this study, of which 23 subjects were terminated early and a total of 92 subjects completed the study.

### Pre-assignment

Screening details:

Participants received OROS methylphenidate once daily between 6:30 am and 9:00 am regardless of meals for 12 weeks during the study period. In case of participants who were taking a drug for Attention Deficit Hyperactivity Disorder (ADHD) treatment other than OROS methylphenidate, a washout period was given for one week or more.

### Period 1

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

### Arms

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | OROS methylphenidate |
|------------------|----------------------|

Arm description:

OROS methylphenidate (or methylphenidate hydrochloride) once daily between 6:30 am and 9:00 am regardless of meals for 12 weeks during the study period.

|  |                               |
|--|-------------------------------|
| Arm type                               | Experimental                  |
| Investigational medicinal product name | METHYLPHENIDATE HYDROCHLORIDE |
| Investigational medicinal product code |                               |
| Other name                             | CONCERTA                      |
| Pharmaceutical forms                   | Capsule                       |
| Routes of administration               | Oral use                      |

Dosage and administration details:

CONCERTA capsule 72 mg orally.

| Number of subjects in period 1 | OROS methylphenidate |
|--------------------------------|----------------------|
| Started                        | 113                  |
| Completed                      | 92                   |
| Not completed                  | 21                   |
| Consent withdrawn by subject   | 8                    |
| Adverse event, non-fatal       | 6                    |
| Lost to follow-up              | 1                    |
| Protocol deviation             | 6                    |

## Baseline characteristics

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | OROS methylphenidate |
|-----------------------|----------------------|

Reporting group description:

OROS methylphenidate (or methylphenidate hydrochloride) once daily between 6:30 am and 9:00 am regardless of meals for 12 weeks during the study period.

| Reporting group values                             | OROS methylphenidate | Total |  |
|--|----------------------|-------|--|
| Number of subjects                                 | 113                  | 113   |  |
| Age categorical                                    |                      |       |  |
| Units: Subjects                                    |                      |       |  |
| In utero   | 0                    | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                    | 0     |  |
| Newborns (0-27 days)                               | 0                    | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                    | 0     |  |
| Children (2-11 years)                              | 0                    | 0     |  |
| Adolescents (12-17 years)                          | 104                  | 104   |  |
| Adults (18-64 years)                               | 9                    | 9     |  |
| From 65-84 years                                   | 0                    | 0     |  |
| 85 years and over                                  | 0                    | 0     |  |
| Age continuous                                     |                      |       |  |
| Units: years                                       |                      |       |  |
| arithmetic mean                                    | 15.2                 |       |  |
| standard deviation                                 | ± 1.43               | -     |  |
| Gender categorical                                 |                      |       |  |
| Units: Subjects                                    |                      |       |  |
| Female   | 27                   | 27    |  |
| Male   | 86                   | 86    |  |

## End points

### End points reporting groups

|  |                      |
|--|----------------------|
| Reporting group title  | OROS methylphenidate |
| Reporting group description:<br>OROS methylphenidate (or methylphenidate hydrochloride) once daily between 6:30 am and 9:00 am regardless of meals for 12 weeks during the study period. |                      |

### Primary: Korean Version of the Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale (K-ARS) Score

|   |   |
|---|---|
| End point title   | Korean Version of the Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale (K-ARS) Score <sup>[1]</sup> |
| End point description:<br>The K-ARS is a rating scale that is used for the ADHD diagnosis and the assessment of treatment efficacy and comprises 18 items in total on the basis of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), each item being rated from 0-3 points. The total score ranges from 0-54 with 0=normal and 54=severe condition. Intent-to-treat (ITT) population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. |   |
| End point type  | Primary   |
| End point timeframe:<br>Baseline and Week 12  |   |

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: Descriptive statistics were done, no inferential statistical analyses were performed

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 113                  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Baseline                             | 27.58 (± 8.92)       |  |  |  |
| Week 12                              | 11.78 (± 7.64)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Clinical Global Impression - Severity (CGI-S) Score

|  |  |
|--|--|
| End point title  | Clinical Global Impression - Severity (CGI-S) Score <sup>[2]</sup> |
| End point description:<br>The CGI-S rating scale is a 7 point global assessment that measures the clinician's impression of the severity of illness exhibited by a participant. A rating of 1 is equivalent to "Normal, not at all ill" and a rating of 7 is equivalent to "Among the most extremely ill participants". Higher scores indicate worsening. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. |  |
| End point type   | Primary  |

End point timeframe:

Baseline and Week 12

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed

| End point values                     | OROS<br>methylphenidate |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 113                     |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) |                         |  |  |  |
| Baseline                             | 4.88 (± 0.79)           |  |  |  |
| Week 12                              | 2.81 (± 1.12)           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Clinical Global Impression - Improvement (CGI-I) Score

|                 |   |
|-----------------|---|
| End point title | Clinical Global Impression - Improvement (CGI-I) Score <sup>[3]</sup> |
|-----------------|---|

End point description:

The CGI-I is a 7-point scale that requires the clinician to assess how much the participant's illness has improved or worsened relative to a baseline state at the beginning of the intervention and rated as: 1=very much improved; 2=much improved; 3=minimally improved; 4=no change; 5=minimally worse; 6=much worse; 7=very much worse. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analysed for this endpoint.

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

End point timeframe:

Week 12

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: Descriptive statistics were done, no inferential statistical analyses were performed

| End point values                     | OROS<br>methylphenidate |  |  |  |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type                   | Reporting group         |  |  |  |
| Number of subjects analysed          | 103                     |  |  |  |
| Units: units on a scale              |                         |  |  |  |
| arithmetic mean (standard deviation) | 2.14 (± 0.75)           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Learning Skill Test (LST) Total Score

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Learning Skill Test (LST) Total Score |
|-----------------|---------------------------------------|

End point description:

The LST measures learning ability of student. This scale is composed of 7 sections: self-control, participation, task accomplishment, reading, writing, test taking and information processing. It consists of 70 items for middle school student (age 13-15 years) and 80 items for high school student (age 16-18 years). Each item is rated on a 5-point Likert scale ranging from 1 (never) to 5 (always). The total score range is 70-350 for middle school version and 80-400 for high school version where higher score indicates better ability for learning. In result analysis, each sub-score and total score was converted to T-score for normalization. The T-score is from 1 to 100 with a mean of 50. Higher score indicates better ability for learning. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 98 <sup>[4]</sup>    |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Baseline                             | 40.97 (± 11.07)      |  |  |  |
| Week 12                              | 49.61 (± 11.57)      |  |  |  |

Notes:

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

## Statistical analyses

No statistical analyses for this end point

## Secondary: Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnostic System (ADS) Test Result for Omission Errors and Commission Errors

|                 |   |
|-----------------|---|
| End point title | Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnostic System (ADS) Test Result for Omission Errors and Commission Errors |
|-----------------|---|

End point description:

The ADS is composed of 4 factors: omission/missing frequency to measure attention dispersibility; false alarm/commission frequency to measure impulse; mean response/reaction time to measure the speed of task processing; and the response variability/standard deviation of response time to measure the consistency of attention. The total value for both, omission errors and commission errors, ranges from 0-100 errors where high value indicates worsening attention. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12



| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 101                  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Omission errors: Baseline            | 58.88 ( $\pm$ 27.35) |  |  |  |
| Omission errors: Week 12             | 57.4 ( $\pm$ 48.79)  |  |  |  |
| Commission errors: Baseline          | 62.39 ( $\pm$ 32.32) |  |  |  |
| Commission errors: Week 12           | 51.7 ( $\pm$ 21.19)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnostic System (ADS) Test Score for Reaction Time and Response Variability

|  |   |
|--|---|
| End point title  | Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnostic System (ADS) Test Score for Reaction Time and Response Variability |
| End point description:<br>The ADS is composed of 4 factors: omission/missing frequency to measure attention dispersibility; false alarm/commission frequency to measure impulse; mean response/reaction time to measure the speed of task processing; and the response variability/standard deviation of response time to measure the consistency of attention. The score range for both, reaction time and response variability, is 0-100. High score indicates worsening attention. If one or over factor's score is over 65 point, the participant is resulted in having attention deficit. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline and Week 12   |   |

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 101                  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Reaction time average: Baseline      | 54.32 ( $\pm$ 15.45) |  |  |  |
| Reaction time average: Week 12       | 49.73 ( $\pm$ 26.33) |  |  |  |

|                                |                      |  |  |  |
|--------------------------------|----------------------|--|--|--|
| Response variability: Baseline | 85.77 ( $\pm$ 60.21) |  |  |  |
| Response variability: Week 12  | 59.42 ( $\pm$ 64.77) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Digit Span Test Score

|                 |                       |
|-----------------|-----------------------|
| End point title | Digit Span Test Score |
|-----------------|-----------------------|

End point description:

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

End point timeframe:

Baseline and Week 12

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 100                  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Forward: Baseline                    | 11.19 ( $\pm$ 2.92)  |  |  |  |
| Forward: Week 12                     | 11.56 ( $\pm$ 2.9)   |  |  |  |
| Backward: Baseline                   | 7.09 ( $\pm$ 2.39)   |  |  |  |
| Backward: Week 12                    | 7.32 ( $\pm$ 2.41)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Finger Window (FW) Test Score

|                 |                               |
|-----------------|-------------------------------|
| End point title | Finger Window (FW) Test Score |
|-----------------|-------------------------------|

End point description:

In Finger Window (FW) test, a participant shows memory of a demonstrated visual pattern using an 8x11 inch plastic template containing 9 asymmetrically located holes. The examiner models a given sequence of holes and asks the participant to imitate the sequence by placing his/her finger through the same holes in the correct order. The total number of correct sequences constitutes the total score which ranges from 0-24 (forward FW) and 0-28 (backward FW) with higher score indicating a more favorable health state. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 100                  |  |  |  |
| Units: units on a scale              |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Forward FW: Baseline                 | 18.42 (± 4.6)        |  |  |  |
| Forward FW: Week 12                  | 19.09 (± 4.49)       |  |  |  |
| Backward FW: Baseline                | 15.59 (± 4.97)       |  |  |  |
| Backward FW: Week 12                 | 17.36 (± 3.84)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Controlled Oral Words Association Test (COWAT) Score

|   |  |
|---|--|
| End point title   | Controlled Oral Words Association Test (COWAT) Score |
| End point description:  |  |
| This test measures the executive function of the frontal lobe and is consisted of examinations of category/meaning fluency and letter/phoneme fluency. It consisted of three 60 second word generation trials in which the participant orally generates as many words as possible that begin with target letters F, A and S. Dependent variables included total number of acceptable words generated for each target letter and total number of words generated across all three letter trials. Total score was calculated as sum of acceptable words generated, with higher scores indicating better verbal fluency. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline and Week 12  |  |

| End point values                     | OROS methylphenidate |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 100                  |  |  |  |
| Units: words                         |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Category/semantic: Baseline          | 29.71 (± 5.86)       |  |  |  |
| Category/semantic: Week 12           | 30.62 (± 6.16)       |  |  |  |
| Letter/phenomic: Baseline            | 28.71 (± 10.82)      |  |  |  |
| Letter/phenomic: Week 12             | 33.78 (± 11.18)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Stroop Test Result for Reaction Time

|                 |                                      |
|-----------------|--------------------------------------|
| End point title | Stroop Test Result for Reaction Time |
|-----------------|--------------------------------------|

End point description:

This test consists of 3 trials: color trial (simple execution), word trial (middle execution) and word-color interference trial (interfering execution). In simple execution, participants have to read the written color names of the words independent of the color of the ink. In middle execution, participants have to read words written in black letters. In interfering experiment, participants have to say the color of the letters independent of the written word. This test estimates spending time for execution. High spending time indicates low ability of suppression of automation. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12

| End point values                               | OROS methylphenidate |  |  |  |
|--|----------------------|--|--|--|
| Subject group type                             | Reporting group      |  |  |  |
| Number of subjects analysed                    | 100                  |  |  |  |
| Units: seconds                                 |                      |  |  |  |
| arithmetic mean (standard deviation)           |                      |  |  |  |
| Simple execution false reaction: Baseline      | 14.78 (± 3.8)        |  |  |  |
| Simple execution false reaction: Week 12       | 13.64 (± 3.27)       |  |  |  |
| Middle execution false reaction: Baseline      | 15.88 (± 3.56)       |  |  |  |
| Middle execution false reaction: Week 12       | 15.04 (± 4.57)       |  |  |  |
| Interfering execution false reaction: Baseline | 22.12 (± 6.18)       |  |  |  |
| Interfering execution time: Week 12            | 19.72 (± 5.63)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Stroop Test Result for False Reaction

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Stroop Test Result for False Reaction |
|-----------------|---------------------------------------|

**End point description:**

This test consists of 3 trials: color trial (simple execution), word trial (middle execution) and word-color interference trial (interfering execution). In simple execution, participants have to read the written color names of the words independent of the color of the ink. In middle execution, participants have to read words written in black letters. In interfering experiment, participants have to say the color of the letters independent of the written word. The total value ranges from 0-24 errors for each execution where high value indicates worsening attention. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12

| End point values                               | OROS methylphenidate |  |  |  |
|--|----------------------|--|--|--|
| Subject group type                             | Reporting group      |  |  |  |
| Number of subjects analysed                    | 100                  |  |  |  |
| Units: errors                                  |                      |  |  |  |
| arithmetic mean (standard deviation)           |                      |  |  |  |
| Simple execution false reaction: Baseline      | 0.4 (± 0.77)         |  |  |  |
| Simple execution false reaction: Week 12       | 0.16 (± 0.39)        |  |  |  |
| Middle execution false reaction: Baseline      | 0.3 (± 0.67)         |  |  |  |
| Middle execution false reaction: Week 12       | 0.2 (± 0.47)         |  |  |  |
| Interfering execution false reaction: Baseline | 1.04 (± 1.29)        |  |  |  |
| Interfering execution false reaction: Week 12  | 0.84 (± 1)           |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Stroop Test Score for Ratio Interference**

|                 |  |
|-----------------|--|
| End point title | Stroop Test Score for Ratio Interference |
|-----------------|--|

**End point description:**

Ratio interference is calculated by dividing simple execution time by interfering execution time. The score range is 0-1. Higher value indicates better ability of suppression of automation. ITT population included all participants who received the study drug at least once, satisfied the inclusion/exclusion criteria and had efficacy assessment data at the Baseline. Here 'N' signifies number of participants analyzed for this end point.

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

End point timeframe:

Baseline and Week 12

|                                      |                             |  |  |  |
|--------------------------------------|-----------------------------|--|--|--|
| <b>End point values</b>              | OROS<br>methylphenidat<br>e |  |  |  |
| Subject group type                   | Reporting group             |  |  |  |
| Number of subjects analysed          | 100                         |  |  |  |
| Units: units on a scale              |                             |  |  |  |
| arithmetic mean (standard deviation) |                             |  |  |  |
| Baseline                             | 0.7 (± 0.19)                |  |  |  |
| Week 12                              | 0.72 (± 0.19)               |  |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | OROS methylphenidate |
|-----------------------|----------------------|

Reporting group description:

OROS methylphenidate (or methylphenidate hydrochloride) once daily between 6:30 am and 9:00 am regardless of meals for 12 weeks during the study period.

| Serious adverse events                            | OROS<br>methylphenidate |  |  |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events |                         |  |  |
| subjects affected / exposed                       | 2 / 113 (1.77%)         |  |  |
| number of deaths (all causes)                     | 0                       |  |  |
| number of deaths resulting from adverse events    | 0                       |  |  |
| Blood and lymphatic system disorders              |                         |  |  |
| Lymphadenitis                                     |                         |  |  |
| subjects affected / exposed                       | 1 / 113 (0.88%)         |  |  |
| occurrences causally related to treatment / all   | 0 / 0                   |  |  |
| deaths causally related to treatment / all        | 0 / 0                   |  |  |
| Infections and infestations                       |                         |  |  |
| Appendicitis                                      |                         |  |  |
| subjects affected / exposed                       | 1 / 113 (0.88%)         |  |  |
| occurrences causally related to treatment / all   | 0 / 0                   |  |  |
| deaths causally related to treatment / all        | 0 / 0                   |  |  |

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

| Non-serious adverse events                            | OROS<br>methylphenidate |  |  |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 98 / 113 (86.73%)       |  |  |
| Cardiac disorders                                     |                         |  |  |

|   |   |  |  |
|---|---|--|--|
| Palpitations<br>subjects affected / exposed<br>occurrences (all)  | 8 / 113 (7.08%)<br>8  |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Somnolence<br>subjects affected / exposed<br>occurrences (all)   | 11 / 113 (9.73%)<br>12<br><br>31 / 113 (27.43%)<br>34<br><br>8 / 113 (7.08%)<br>8   |  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Irritability<br>subjects affected / exposed<br>occurrences (all)  | 13 / 113 (11.50%)<br>14<br><br>16 / 113 (14.16%)<br>18  |  |  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Stomach discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 19 / 113 (16.81%)<br>19<br><br>6 / 113 (5.31%)<br>7<br><br>32 / 113 (28.32%)<br>38<br><br>15 / 113 (13.27%)<br>15<br><br>7 / 113 (6.19%)<br>8 |  |  |



|   |                   |  |  |
|---|-------------------|--|--|
| Psychiatric disorders                           |                   |  |  |
| Anger   |                   |  |  |
| subjects affected / exposed                     | 6 / 113 (5.31%)   |  |  |
| occurrences (all)                               | 6                 |  |  |
| Anxiety   |                   |  |  |
| subjects affected / exposed                     | 9 / 113 (7.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Depression                                      |                   |  |  |
| subjects affected / exposed                     | 9 / 113 (7.96%)   |  |  |
| occurrences (all)                               | 9                 |  |  |
| Insomnia  |                   |  |  |
| subjects affected / exposed                     | 37 / 113 (32.74%) |  |  |
| occurrences (all)                               | 40                |  |  |
| Nervousness                                     |                   |  |  |
| subjects affected / exposed                     | 7 / 113 (6.19%)   |  |  |
| occurrences (all)                               | 7                 |  |  |
| Musculoskeletal and connective tissue disorders |                   |  |  |
| Myalgia   |                   |  |  |
| subjects affected / exposed                     | 6 / 113 (5.31%)   |  |  |
| occurrences (all)                               | 6                 |  |  |
| Infections and infestations                     |                   |  |  |
| Nasopharyngitis                                 |                   |  |  |
| subjects affected / exposed                     | 19 / 113 (16.81%) |  |  |
| occurrences (all)                               | 22                |  |  |
| Metabolism and nutrition disorders              |                   |  |  |
| Decreased appetite                              |                   |  |  |
| subjects affected / exposed                     | 66 / 113 (58.41%) |  |  |
| occurrences (all)                               | 75                |  |  |

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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| Subject or investigator bias due to placebo effect could not be excluded because this study was conducted in an open-label, single-arm design and learning skill of subjects could not be evaluated by parents and teachers but only depended on subjects. |
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Notes: