

**Clinical trial results:****An Open-Label Study of the Efficacy of Atomoxetine Hydrochloride on Quality of Life of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder with or without comorbid conditions**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

**Summary**

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2005-005701-32  |
| Trial protocol           | IT              |
| Global end of trial date | 06 October 2008 |

**Results information**

|                                   |                                                                               |
|-----------------------------------|-------------------------------------------------------------------------------|
| Result version number             | v2 (current)                                                                  |
| This version publication date     | 24 July 2016                                                                  |
| First version publication date    | 05 August 2015                                                                |
| Version creation reason           | • Correction of full data set<br>Correction needed to Full Data Set           |
| Summary attachment (see zip file) | EudraCT Full Data Set Results PDF<br>(LYDS_RR_Approval_EudraCT_16JUL2015.pdf) |

**Trial information****Trial identification**

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | B4Z-IT-LYDS |
|-----------------------|-------------|

**Additional study identifiers**

|                                    |                                              |
|------------------------------------|----------------------------------------------|
| ISRCTN number                      | -                                            |
| ClinicalTrials.gov id (NCT number) | NCT00320528                                  |
| WHO universal trial number (UTN)   | -                                            |
| Other trial identifiers            | Trial Number: 9867, Trial Alias: B4Z-IT-LYDS |

Notes:

**Sponsors**

|                              |                                                                   |
|------------------------------|-------------------------------------------------------------------|
| Sponsor organisation name    | Eli Lilly and Company                                             |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285    |
| Public contact               | Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLILLY,  |
| Scientific contact           | Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

Notes:

**Paediatric regulatory details**

|                                                                      |    |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 06 October 2008 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 06 October 2008 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

Please Note: The Agency is aware of a bug when posting the summary of the clinical trial results: the order in which the arms/reporting groups are provided may not be maintained when the results are viewed online, downloaded as a PDF or downloaded as a XML. This inconsistency may exist in other areas like subject disposition, end points, baseline characteristics etc. where the reporting groups are referenced. Please see attached results summary for correctly reported baseline characteristics data.

Main Objective: This study aims to assess the effectiveness of atomoxetine on psychosocial functioning and emotional well being of children and adolescents with Attention-Deficit/Hyperactivity Disorder (ADHD) and to evaluate whether and in what measure the presence of comorbid conditions (internalizing and externalizing disorders) influences atomoxetine's ability to improve the quality of life of ADHD subjects.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 29 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 | Italy: 269 |
| Worldwide total number of subjects   | 269        |
| EEA total number of subjects         | 269        |

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)                    | 187 |
| Adolescents (12-17 years)                | 82  |
| Adults (18-64 years)                     | 0   |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

No text entered.

### Pre-assignment

Screening details:

Study Period I was a 3-day screening period. Study Period II was 12 weeks long. Study Period III was an optional additional 12 week open-label extension. Results are presented for Period II (patients who received at least one dose of study drug).

### Period 1

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

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Pure ADHD (Period II) |

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                  |                                          |
|------------------|------------------------------------------|
| <b>Arm title</b> | ADHD+Internalizing Disorders (Period II) |
|------------------|------------------------------------------|

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                  |                                          |
|------------------|------------------------------------------|
| <b>Arm title</b> | ADHD+Externalizing Disorders (Period II) |
|------------------|------------------------------------------|

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

| Number of subjects in period 1           | Pure ADHD (Period II) | ADHD+Internalizing Disorders (Period II) | ADHD+Externalizing Disorders (Period II) |
|------------------------------------------|-----------------------|------------------------------------------|------------------------------------------|
| Started                                  | 98                    | 41                                       | 130                                      |
| Received at Least One Dose of Study Drug | 97                    | 38                                       | 128                                      |
| Completed                                | 87                    | 31                                       | 108                                      |
| Not completed                            | 11                    | 10                                       | 22                                       |
| Parent/Caregiver Decision                | 8                     | 3                                        | 11                                       |
| Consent withdrawn by subject             | -                     | 1                                        | 1                                        |
| Adverse event, non-fatal                 | 3                     | 4                                        | 8                                        |
| Entry Criteria Exclusion                 | -                     | 2                                        | 2                                        |

## Period 2

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

## Arms

|                              |                        |
|------------------------------|------------------------|
| Are arms mutually exclusive? | No                     |
| <b>Arm title</b>             | Pure ADHD (Period III) |

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                  |                                           |
|------------------|-------------------------------------------|
| <b>Arm title</b> | ADHD+Internalizing Disorders (Period III) |
|------------------|-------------------------------------------|

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                  |                                           |
|------------------|-------------------------------------------|
| <b>Arm title</b> | ADHD+Externalizing Disorders (Period III) |
|------------------|-------------------------------------------|

Arm description:

Attention-Deficit/Hyperactivity Disorder (ADHD) plus externalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | atomoxetine         |
| Investigational medicinal product code |                     |
| Other name                             | LY139603, Strattera |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks

| Number of subjects in period 2     | Pure ADHD (Period III) | ADHD+Internalizing Disorders (Period III) | ADHD+Externalizing Disorders (Period III) |
|------------------------------------|------------------------|-------------------------------------------|-------------------------------------------|
|                                    |                        |                                           |                                           |
| Started                            | 87                     | 31                                        | 108                                       |
| Completed                          | 0                      | 0                                         | 2                                         |
| Not completed                      | 87                     | 31                                        | 106                                       |
| Parent/Caregiver Decision          | 14                     | 3                                         | 11                                        |
| Consent withdrawn by subject       | 1                      | -                                         | -                                         |
| Atomoxetine Commercially Available | 68                     | 25                                        | 90                                        |
| Physician decision                 | -                      | 1                                         | 2                                         |
| Adverse event, non-fatal           | 1                      | -                                         | -                                         |
| Withdrawal by Subject              | -                      | 1                                         | 2                                         |
| Sponsor Decision                   | -                      | -                                         | 1                                         |
| Protocol Violation                 | -                      | 1                                         | -                                         |
| Lost to follow-up                  | 1                      | -                                         | -                                         |
| Lack of efficacy                   | 2                      | -                                         | -                                         |



## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                 |                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                           | Pure ADHD (Period II)                    |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks                                    |                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Internalizing Disorders (Period II) |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine:... more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless |                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Externalizing Disorders (Period II) |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks             |                                          |

| Reporting group values             | Pure ADHD (Period II) | ADHD+Internalizing Disorders (Period II) | ADHD+Externalizing Disorders (Period II) |
|------------------------------------|-----------------------|------------------------------------------|------------------------------------------|
| Number of subjects                 | 98                    | 41                                       | 130                                      |
| Age categorical<br>Units: Subjects |                       |                                          |                                          |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                 |                 |              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-----------------|--------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 10.12<br>± 2.51 | 10.42<br>± 2.41 | 10<br>± 2.57 |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                 |                 |              |
| Female                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 14              | 3               | 9            |
| Male                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 83              | 35              | 119          |
| Not Recorded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1               | 3               | 2            |
| Region of Enrollment<br>Units: Subjects                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                 |                 |              |
| Italy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 98              | 41              | 130          |
| Race/Ethnicity<br>Units: Subjects                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                 |                 |              |
| Caucasian                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 90              | 36              | 124          |
| Hispanic                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1               | 2               | 2            |
| African                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 3               | 0               | 0            |
| Native American                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1               | 0               | 2            |
| East Asian                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 2               | 0               | 0            |
| Not Recorded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1               | 3               | 2            |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Achievement Domain (N=96, N=33, N=121)                                                                                                                                                                                                                                                                                                                                                                                                                       |                 |                 |              |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to |                 |                 |              |



|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |         |         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|---------|---------|
| 67.7. Higher scores mean greater health or level of functioning in achievement.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |         |         |
| Units: T-Score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 29.27   | 27.72   | 25.83   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 7.89  | ± 7.73  | ± 7.6   |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Satisfaction Domain (N=96, N=24, N=122)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |         |         |         |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |         |         |         |
| Units: T-Score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 39.26   | 30.11   | 31.69   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 13.89 | ± 14.83 | ± 14.78 |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Comfort Domain (N=96, N=35, N=122)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |         |         |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |         |         |         |
| Units: T-Score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 51.31   | 46.76   | 44.74   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 9.4   | ± 12.28 | ± 9.38  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Resilience Domain (N=96, N=34, N=123)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |         |         |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |         |         |         |
| Units: T-Score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 39.34   | 34.96   | 31.4    |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 10.15 | ± 10.89 | ± 11.85 |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Risk Avoidance (N=96, N=33, N=121)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |         |         |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |         |         |         |
| Units: T-Score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 32.03   | 30.48   | 22.85   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 9.7   | ± 12.29 | ± 12    |
| Children's Depression Rating Scale-Revised (CDRS-R)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |         |         |
| Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression.                                                                                                                                                                                                                                               |         |         |         |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 37.93   | 43.76   | 43.06   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ± 12.26 | ± 13.48 | ± 13.69 |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |        |        |        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|--------|--------|
| Clinical Global Impression-Attention Deficit Hyperactivity Disorder-Severity Scale (CGI-ADHD-S)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |        |        |        |
| Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients).                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 4.64   | 4.97   | 4.98   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 0.79 | ± 0.79 | ± 0.78 |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |        |        |        |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                                                                                                                                                                                                                                                                                          |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 5.97   | 4.97   | 8.62   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 4.93 | ± 4.66 | ± 4.83 |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) Cognitive Problems                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |        |        |        |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                                                                                                                                                                                                                                                                                          |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 7.86   | 7.68   | 7.96   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 3.73 | ± 3.8  | ± 3.61 |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |        |        |        |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                                                                                                                                                                                                                                                                                          |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 11.38  | 12.03  | 14.67  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 6.09 | ± 5.21 | ± 5.15 |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) ADHD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |        |        |        |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                                                                                                                                                                                                                                                                                          |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 22.14  | 22.94  | 25.18  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 6.86 | ± 6.01 | ± 6.07 |
| Pediatric Anxiety Rating Scale (PARS)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |        |        |        |
| The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25 (extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation.                                                                                                                                                        |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 2.5    | 7.5    | 4.67   |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 2.67 | ± 5.68 | ± 5.12 |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Inattention Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |        |        |        |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |        |        |        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|--------|--------|
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 20.28  | 21.03  | 21.87  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 4.19 | ± 3.72 | ± 3.48 |
| SNAP-IV Hyperactivity/Impulsivity Subscale (N=97, N=38)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 17.21  | 19.66  | 21.04  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 6.1  | ± 5.54 | ± 3.48 |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Combined Type Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |        |        |        |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 37.48  | 40.68  | 42.91  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 7.78 | ± 7.87 | ± 5.51 |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Oppositional Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |        |        |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |        |        |        |
| Units: units on a scale                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |        |        |
| arithmetic mean                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 10.15  | 12.32  | 17.99  |
| standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ± 4.54 | ± 4.67 | ± 3.57 |

|                               |       |  |  |
|-------------------------------|-------|--|--|
| <b>Reporting group values</b> | Total |  |  |
| Number of subjects            | 269   |  |  |
| Age categorical               |       |  |  |
| Units: Subjects               |       |  |  |

|                      |     |  |  |
|----------------------|-----|--|--|
| Age continuous       |     |  |  |
| Units: years         |     |  |  |
| arithmetic mean      |     |  |  |
| standard deviation   | -   |  |  |
| Gender categorical   |     |  |  |
| Units: Subjects      |     |  |  |
| Female               | 26  |  |  |
| Male                 | 237 |  |  |
| Not Recorded         | 6   |  |  |
| Region of Enrollment |     |  |  |
| Units: Subjects      |     |  |  |
| Italy                | 269 |  |  |
| Race/Ethnicity       |     |  |  |
| Units: Subjects      |     |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |     |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|--|--|
| Caucasian                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 250 |  |  |
| Hispanic                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 5   |  |  |
| African                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 3   |  |  |
| Native American                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 3   |  |  |
| East Asian                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 2   |  |  |
| Not Recorded                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 6   |  |  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Achievement Domain (N=96, N=33, N=121)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |     |  |  |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |     |  |  |
| Units: T-Score<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | -   |  |  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Satisfaction Domain (N=96, N=24, N=122)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |     |  |  |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |     |  |  |
| Units: T-Score<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | -   |  |  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Comfort Domain (N=96, N=35, N=122)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |     |  |  |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |     |  |  |
| Units: T-Score<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | -   |  |  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Resilience Domain (N=96, N=34, N=123)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |     |  |  |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |     |  |  |
| Units: T-Score<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | -   |  |  |
| Child Health and Illness Profile - Child Edition (CHIP-CE) - Risk Avoidance (N=96, N=33, N=121)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |     |  |  |
| Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |     |  |  |

|                                                                                                                                                                                                                                                                                                                                                             |   |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|--|--|
| 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement.                                                                                                                                                                           |   |  |  |
| Units: T-Score<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                     |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Children's Depression Rating Scale-Revised (CDRS-R)                                                                                                                                                                                                                                                                                                         |   |  |  |
| Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression. |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Clinical Global Impression-Attention Deficit Hyperactivity Disorder-Severity Scale (CGI-ADHD-S)                                                                                                                                                                                                                                                             |   |  |  |
| Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients).                                                                                                                                                                                                                   |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)                                                                                                                                                                                                                                                                                                 |   |  |  |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                               |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)<br>Cognitive Problems                                                                                                                                                                                                                                                                           |   |  |  |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                               |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S)                                                                                                                                                                                                                                                                                                 |   |  |  |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                               |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Conners' Teacher Rating Scale-Revised:Short Form (CTRS-R:S) ADHD                                                                                                                                                                                                                                                                                            |   |  |  |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index.                                                               |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                            |   |  |  |
|                                                                                                                                                                                                                                                                                                                                                             | - |  |  |
| Pediatric Anxiety Rating Scale (PARS)                                                                                                                                                                                                                                                                                                                       |   |  |  |
| The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25                                                             |   |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|--|--|
| (extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation.                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | - |  |  |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Inattention Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |  |  |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | - |  |  |
| SNAP-IV Hyperactivity/Impulsivity Subscale (N=97, N=38)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |  |  |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | - |  |  |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Combined Type Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |   |  |  |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | - |  |  |
| Swanson, Nolan, and Pelham Rating Scale Revised (SNAP-IV) Oppositional Subscale (N=97, N=38, N=127)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |  |  |
| The SNAP-IV is a 26-item scale that includes 1 item for each of the 18 symptoms contained in the DSM-IV diagnosis of ADHD and 1 item for each of the 8 symptoms contained in the DSM-IV diagnosis of ODD. Each item is score on 0 to 3 scale (0 = "Not at All", 1 = "Just a Little", 2 = "Pretty Much", 3 = "Very Much"). The SNAP-IV yields scores in three domains: Inattention (items 1-9: subscore range=0-27), Hyperactivity/impulsivity (items 10-18: subscale range=0-27), and Oppositional (items 19-26: subscale range=0-24). Combined type (inattention + hyperactivity/impulsivity) scores range from 0-54. |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | - |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                 |                                           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                           | Pure ADHD (Period II)                     |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks                                    |                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Internalizing Disorders (Period II)  |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine:... more 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeksless |                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Externalizing Disorders (Period II)  |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks             |                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                           | Pure ADHD (Period III)                    |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) alone. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks                                    |                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Internalizing Disorders (Period III) |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus internalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks             |                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                           | ADHD+Externalizing Disorders (Period III) |
| Reporting group description:<br>Attention-Deficit/Hyperactivity Disorder (ADHD) plus externalizing disorders. Received atomoxetine: 0.5 milligrams per kilogram per day (mg/kg/day), by mouth (PO) for 1 week then 1.2 mg/kg/day, PO for 11 weeks followed by up to 1.4 mg/kg/day, PO for up to 12 additional weeks             |                                           |

### Primary: 1: Change From Baseline to 12 Week Endpoint in Child Health and Illness Profile - Child Edition (CHIP-CE), Achievement Domain

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1: Change From Baseline to 12 Week Endpoint in Child Health and Illness Profile - Child Edition (CHIP-CE), Achievement Domain |
| End point description:<br>Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains and subdomains having a mean score of 50 and standard deviation of 10. Standard scores are expressed in standard deviation units. Achievement Domain Range = -3.1 to 67.7. Higher scores mean greater health or level of functioning in achievement. |                                                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Primary                                                                                                                       |
| End point timeframe:<br>Baseline, 12 Weeks                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                               |

| End point values                          | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|-------------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                        | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed               | 83 <sup>[1]</sup>        | 28 <sup>[2]</sup>                               | 97 <sup>[3]</sup>                               |  |
| Units: T-Score                            |                          |                                                 |                                                 |  |
| arithmetic mean (confidence interval 95%) | 2.65 (0.93 to 4.37)      | 0.51 (-1.38 to 2.39)                            | 3.89 (2.22 to 5.57)                             |  |

Notes:

[1] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

[2] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

[3] - Number of patients with baseline and at least one nonmissing post-baseline measurement.

## Statistical analyses

| Statistical analysis title              | Statistical Analysis for End Point 1                                                                        |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | ADHD+Internalizing Disorders (Period II) v ADHD+Externalizing Disorders (Period II) v Pure ADHD (Period II) |
| Number of subjects included in analysis | 208                                                                                                         |
| Analysis specification                  | Pre-specified                                                                                               |
| Analysis type                           | other                                                                                                       |
| P-value                                 | < 0.05                                                                                                      |
| Method                                  | LOCF analysis                                                                                               |

## Secondary: 2: Change From Baseline to 12 Week Endpoint in the Attention-Deficit/Hyperactivity Disorder (ADHD) Subscales of 18-Item Swanson, Nolan and Pelham Rating Scale (SNAP-IV)

|                 |                                                                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | 2: Change From Baseline to 12 Week Endpoint in the Attention-Deficit/Hyperactivity Disorder (ADHD) Subscales of 18-Item Swanson, Nolan and Pelham Rating Scale (SNAP-IV) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Items from the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for ADHD are included for the two subsets of symptoms: inattention (items #1-#9: total score=0-27) and hyperactivity/impulsivity (items #11-#19: total score=0-27). The SNAP-IV is based on a 0 (not at all) to 3 (very much) rating scale. Total combined type (inattention plus hyperactivity/impulsivity) subscale scores range from 0 to 54.

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

End point timeframe:

Baseline, 12 Weeks

| End point values                          | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|-------------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                        | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed               | 90                       | 33                                              | 111                                             |  |
| Units: units on a scale                   |                          |                                                 |                                                 |  |
| arithmetic mean (confidence interval 95%) |                          |                                                 |                                                 |  |
| Inattention Subscale                      | -5.88 (-7.25 to -5.13)   | -5.52 (-7.34 to -3.69)                          | -7.58 (-8.69 to -6.46)                          |  |



|                                    |                        |                        |                        |  |
|------------------------------------|------------------------|------------------------|------------------------|--|
| Hyperactivity/Impulsivity Subscale | -12.1 (-13.9 to -10.3) | -5.67 (-7.41 to -3.92) | -8.08 (-9.09 to -7.07) |  |
| Combined Type (ADHD) Subscale      | -6.19 (-6.97 to -4.78) | -11.2 (-14.4 to -7.92) | -15.7 (-17.6 to -13.7) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3: Change From Baseline to 12 Week Endpoint in Clinical Global Impressions-ADHD-Severity (CGI-ADHD-S)

|                        |                                                                                                                                           |
|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | 3: Change From Baseline to 12 Week Endpoint in Clinical Global Impressions-ADHD-Severity (CGI-ADHD-S)                                     |
| End point description: | Measures severity of the patient's overall severity of ADHD symptoms (1=normal, not at all ill; 7=among the most extremely ill patients). |
| End point type         | Secondary                                                                                                                                 |
| End point timeframe:   | Baseline, 12 Weeks                                                                                                                        |

| End point values                          | Pure ADHD (Period II)  | ADHD+Internalizing Disorders (Period II) | ADHD+Externalizing Disorders (Period II) |  |
|-------------------------------------------|------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                        | Reporting group        | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed               | 88                     | 32                                       | 112                                      |  |
| Units: units on a scale                   |                        |                                          |                                          |  |
| arithmetic mean (confidence interval 95%) | -1.23 (-1.46 to -0.99) | -1.63 (-1.99 to -1.26)                   | -1.42 (-1.63 to -1.21)                   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 4: Change From Baseline to 12 Week Endpoint in CHIP-CE Satisfaction, Comfort, Resilience and Risk Avoidance Domains

|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | 4: Change From Baseline to 12 Week Endpoint in CHIP-CE Satisfaction, Comfort, Resilience and Risk Avoidance Domains                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| End point description: | Parent-rated assessment of a child's health status and level of functioning. It consists of 76 items. The majority of items assess frequency of activities or feelings using a five-point response format (for example, 'how good is your child at making friends?' 1=never, 5=always). Standard scores (t-value) were established, with all domains having a mean score of 50 and standard deviation of 10. Satisfaction range=-25.7 to 66.3; Comfort=-28.6 to 67.2; Resilience=-36.3 to 71.8; Risk Avoidance=-23.5 to 62.5. Higher scores mean greater health or level of functioning in that domain. |
| End point type         | Secondary                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| End point timeframe:   | Baseline, 12 Weeks                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |

| <b>End point values</b>                      | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|----------------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                           | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed                  | 97                       | 38                                              | 128                                             |  |
| Units: T-Score                               |                          |                                                 |                                                 |  |
| arithmetic mean (confidence interval<br>95%) |                          |                                                 |                                                 |  |
| Satisfaction Domain (N=88, N=31,<br>N=105)   | 2.14 (-0.06 to<br>4.34)  | 0.81 (-3.33 to<br>4.95)                         | 3.78 (1.18 to<br>6.39)                          |  |
| Comfort Domain (N=86, N=28, N=103)           | 1.01 (-0.88 to<br>2.9)   | 5.72 (1.24 to<br>10.19)                         | 4.94 (3.14 to<br>6.73)                          |  |
| Resilience Domain (N=87, N=30,<br>N=106)     | 1.21 (-0.85 to<br>3.27)  | 2.18 (-1.31 to<br>5.67)                         | 3.07 (1.1 to<br>5.03)                           |  |
| Risk Avoidance Domain (N=82, N=28,<br>N=94)  | 4.72 (2.93 to<br>6.51)   | 5.7 (1.96 to<br>9.45)                           | 9.88 (7.88 to<br>11.88)                         |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 5: Change From Baseline to 12 Week Endpoint in Pediatric Anxiety Rating Scale (PARS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 5: Change From Baseline to 12 Week Endpoint in Pediatric Anxiety Rating Scale (PARS) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                      |
| The Pediatric Anxiety Rating Scale (PARS) is used to rate the severity of anxiety in children and adolescents, ages 6 to 17 years. The total score for the PARS is derived by summing 5 of the 7 severity/impairment/interference items (2,3,5,6,7). The total score ranges from 0 (none) to 25 (extreme severity). Items 1 (overall number of anxiety symptoms) and 4 (overall severity of physical symptoms) are not included in the total score calculation. |                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Secondary                                                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                      |
| Baseline, 12 Weeks                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                      |

| <b>End point values</b>                      | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|----------------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                           | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed                  | 89                       | 33                                              | 112                                             |  |
| Units: units on a scale                      |                          |                                                 |                                                 |  |
| arithmetic mean (confidence interval<br>95%) | -0.18 (-0.7 to<br>0.34)  | -1.88 (-3.4 to -<br>0.36)                       | -1.18 (-1.9 to -<br>0.46)                       |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 6: Change From Baseline to 12 Week Endpoint in Children's Depression Rating Scale-Revised (CDRS-R)

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | 6: Change From Baseline to 12 Week Endpoint in Children's Depression Rating Scale-Revised (CDRS-R) |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Measures presence and severity of depression. Consists of 17 items scored on a 1-5 or 1-7 scale. A rating of 1 indicates normal, thus the minimum score is 17. The maximum score is 113. In general, scores below 20 indicate an absence of depression; scores of 20 or 30 indicate borderline depression; scores of 40 to 60 indicate moderate depression.

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

End point timeframe:

Baseline, 12 Weeks

| End point values                             | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|----------------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                           | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed                  | 97                       | 38                                              | 128                                             |  |
| Units: units on a scale                      |                          |                                                 |                                                 |  |
| arithmetic mean (confidence interval<br>95%) | -1.6 (-3.54 to<br>0.34)  | -2.56 (-6.38 to<br>1.25)                        | -3.13 (-4.64 to<br>-1.62)                       |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 7: Change From Baseline to 12 Week Endpoint in SNAP-IV Oppositional Scale

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | 7: Change From Baseline to 12 Week Endpoint in SNAP-IV Oppositional Scale |
|-----------------|---------------------------------------------------------------------------|

End point description:

Items are included from the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for Oppositional Defiant Disorder. The SNAP-IV is based on a 0 (not at all) to 3 (very much) rating scale. Total subscale scores range from 0 to 24.

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

End point timeframe:

Baseline, 12 Weeks

| End point values                             | Pure ADHD<br>(Period II)  | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|----------------------------------------------|---------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                           | Reporting group           | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed                  | 90                        | 33                                              | 111                                             |  |
| Units: units on a scale                      |                           |                                                 |                                                 |  |
| arithmetic mean (confidence interval<br>95%) | -2.01 (-2.86 to<br>-1.16) | -2.12 (-3.95 to<br>-0.29)                       | -5.54 (-6.43 to<br>-4.65)                       |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 8: Change From Baseline to 12 Week Endpoint in Adolescent Symptom Inventory-4: Parent Checklist (ASI-4)

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| End point title | 8: Change From Baseline to 12 Week Endpoint in Adolescent Symptom Inventory-4: Parent Checklist (ASI-4) |
|-----------------|---------------------------------------------------------------------------------------------------------|

End point description:

Parent-completed ASI-4 contains 120 items on 18 emotional and behavioral disorders in adolescents (12-18 years old). Item score range:0 (no symptoms) to 3 (maximum impairment). Categories: A=ADHD (0-54); B=Conduct (0-60); C=Oppositional Defiant (0-24); D=Generalized Anxiety (0-18); E=Specific Phobia/Panic Attack/Obsessions/Compulsions/Somatization (0-30); F=Social Phobia (0-6); G=Separation Anxiety (0-24); H=Schizoid Personality (0-9); I=Schizophrenia (0-6); J=Enuresis (0-18); K=Major Depressive (0-42); L=Bipolar (0-27); M=Anorexia (0-12); N=Bulimia (0-12); O=Substance Abuse (0-18).

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

End point timeframe:

Baseline, 12 Weeks

| End point values                     | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|--------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                   | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed          | 26                       | 10                                              | 30                                              |  |
| Units: units on a scale              |                          |                                                 |                                                 |  |
| arithmetic mean (standard deviation) |                          |                                                 |                                                 |  |
| Category A - Baseline                | 32.73 (±<br>11.42)       | 38.33 (±<br>10.32)                              | 38.13 (± 8.3)                                   |  |
| Category A - Change from Baseline    | -11.4 (± 9.88)           | -10.4 (±<br>11.55)                              | -11.6 (± 9.5)                                   |  |
| Category B - Baseline                | 4.04 (± 4.25)            | 6 (± 5.62)                                      | 10.8 (± 5.41)                                   |  |
| Category B - Change from Baseline    | -0.73 (± 2.92)           | -0.6 (± 5.83)                                   | -5.57 (± 5.58)                                  |  |
| Category C- Baseline                 | 7.92 (± 4.77)            | 10.5 (± 3.72)                                   | 15.6 (± 5.24)                                   |  |
| Category C - Change from Baseline    | -0.88 (± 3.85)           | -1.4 (± 6.15)                                   | -5.47 (± 5.51)                                  |  |
| Category D- Baseline                 | 4.73 (± 3.14)            | 9.2 (± 3.58)                                    | 8.37 (± 3.54)                                   |  |
| Category D - Change from Baseline    | -0.58 (± 3.09)           | -1.7 (± 3.65)                                   | -2.97 (± 3.67)                                  |  |
| Category E- Baseline                 | 3.58 (± 4)               | 7.6 (± 7.85)                                    | 3.63 (± 3.16)                                   |  |
| Category E - Change from Baseline    | -0.38 (± 4.01)           | -4.5 (± 8.72)                                   | -1.3 (± 2.35)                                   |  |
| Category F- Baseline                 | 1.19 (± 1.27)            | 2.6 (± 1.43)                                    | 1.2 (± 1.37)                                    |  |
| Category F - Change from Baseline    | -0.58 (± 0.81)           | -1.4 (± 1.43)                                   | -0.53 (± 1.25)                                  |  |
| Category G- Baseline                 | 2.27 (± 3.5)             | 4.5 (± 5.25)                                    | 2.1 (± 2.63)                                    |  |

|                                   |                |               |                |  |
|-----------------------------------|----------------|---------------|----------------|--|
| Category G - Change from Baseline | -0.46 (± 2.49) | -3.2 (± 4.71) | -0.97 (± 2.4)  |  |
| Category H- Baseline              | 0.73 (± 1.28)  | 1.6 (± 2.27)  | 1.7 (± 1.74)   |  |
| Category H - Change from Baseline | -0.38 (± 1.2)  | 0.2 (± 2.86)  | -0.67 (± 1.69) |  |
| Category I- Baseline              | 1 (± 1.92)     | 3.2 (± 3.65)  | 2.13 (± 2.22)  |  |
| Category I - Change from Baseline | -0.19 (± 0.8)  | -1.3 (± 3.89) | -0.93 (± 1.7)  |  |
| Category J- Baseline              | 0.42 (± 0.99)  | 0.4 (± 0.97)  | 0.5 (± 0.78)   |  |
| Category J - Change from Baseline | 0 (± 0.69)     | -0.3 (± 0.67) | -0.23 (± 0.43) |  |
| Category K- Baseline              | 3.73 (± 3.99)  | 4.9 (± 2.85)  | 4.23 (± 4.05)  |  |
| Category K - Change from Baseline | -1.04 (± 2.9)  | -1 (± 3.5)    | -1.6 (± 3.5)   |  |
| Category L- Baseline              | 3.54 (± 4.68)  | 5.1 (± 5)     | 6.03 (± 5.02)  |  |
| Category L - Change from Baseline | -1.08 (± 3.46) | -0.2 (± 6.03) | -1.97 (± 4.3)  |  |
| Category M- Baseline              | 0.73 (± 1.22)  | 1.3 (± 2.06)  | 0.5 (± 1.41)   |  |
| Category M - Change from Baseline | 0.15 (± 1.08)  | -0.1 (± 3.21) | 0.3 (± 1.39)   |  |
| Category N- Baseline              | 1.31 (± 1.54)  | 2.2 (± 3.05)  | 2.3 (± 1.84)   |  |
| Category N - Change from Baseline | -0.38 (± 1.7)  | -0.9 (± 2.23) | -0.8 (± 1.49)  |  |
| Category O- Baseline              | 0.23 (± 0.71)  | 0.3 (± 0.95)  | 0.53 (± 0.97)  |  |
| Category O - Change from Baseline | 0.15 (± 0.37)  | -0.2 (± 0.63) | -0.13 (± 0.51) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 9: Change From Baseline to 12 Week Endpoint in Child Symptom Inventory-4: Parent Checklist (CSI-4)

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | 9: Change From Baseline to 12 Week Endpoint in Child Symptom Inventory-4: Parent Checklist (CSI-4) |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

The CSI-4 contains 97 items that screen for 15 emotional and behavioral disorders in children between 5 and 12 years old. Item score range:0 (no symptoms) to 3 (maximum impairment). Categories: A=ADHD (0-54); B=Conduct (0-60); C=Oppositional Defiant (0-24); D=Generalized Anxiety (0-18); E=Specific Phobia/Panic Attack/Obsessions/Compulsions/Somatization (0-30); F=Social Phobia (0-6); G=Separation Anxiety (0-24); H=Schizoid Personality (0-9); I=Schizophrenia (0-6); J=Enuresis (0-18).

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

End point timeframe:

Baseline, 12 Weeks

| End point values                     | Pure ADHD<br>(Period II) | ADHD+Internal<br>izing Disorders<br>(Period II) | ADHD+Externa<br>lizing Disorders<br>(Period II) |  |
|--------------------------------------|--------------------------|-------------------------------------------------|-------------------------------------------------|--|
| Subject group type                   | Reporting group          | Reporting group                                 | Reporting group                                 |  |
| Number of subjects analysed          | 58                       | 22                                              | 78                                              |  |
| Units: units on a scale              |                          |                                                 |                                                 |  |
| arithmetic mean (standard deviation) |                          |                                                 |                                                 |  |
| Category A - Baseline                | 34 (± 10.43)             | 36 (± 9.32)                                     | 38.95 (± 8.68)                                  |  |
| Category A - Change from Baseline    | -10.6 (± 9.76)           | -9.68 (± 9.54)                                  | -12.7 (± 12.06)                                 |  |
| Category B - Baseline                | 9.29 (± 4.72)            | 11.05 (± 4.13)                                  | 15.65 (± 4.4)                                   |  |
| Category B - Change from Baseline    | -2.12 (± 3.88)           | -1.14 (± 5.25)                                  | -3.76 (± 5.56)                                  |  |
| Category C - Baseline                | 2.1 (± 2.44)             | 2.23 (± 2.25)                                   | 4.63 (± 3.69)                                   |  |

|                                   |                |                |                |  |
|-----------------------------------|----------------|----------------|----------------|--|
| Category C - Change from Baseline | -0.88 (± 2.11) | -0.05 (± 3.06) | -1.99 (± 3.17) |  |
| Category D - Baseline             | 5.83 (± 3.37)  | 8.23 (± 3.96)  | 7.41 (± 3.94)  |  |
| Category D - Change from Baseline | -0.84 (± 3.16) | -2.23 (± 3.01) | -1.63 (± 3.86) |  |
| Category E - Baseline             | 2.07 (± 1.87)  | 2.09 (± 1.95)  | 2.79 (± 2.69)  |  |
| Category E - Change from Baseline | -0.38 (± 1.9)  | -0.41 (± 1.75) | -0.85 (± 2.43) |  |
| Category F - Baseline             | 0.48 (± 0.86)  | 0.32 (± 0.57)  | 0.91 (± 1.35)  |  |
| Category F - Change from Baseline | -0.17 (± 0.94) | -0.14 (± 0.64) | -0.24 (± 1.28) |  |
| Category G - Baseline             | 3.02 (± 2.7)   | 4.05 (± 2.79)  | 3.51 (± 3.3)   |  |
| Category G - Change from Baseline | -0.62 (± 2.4)  | -0.91 (± 2)    | -0.46 (± 2.52) |  |
| Category H - Baseline             | 3.66 (± 4.14)  | 4.64 (± 4.02)  | 4.45 (± 4.39)  |  |
| Category H - Change from Baseline | -1.1 (± 2.21)  | -1.09 (± 2.93) | -1.54 (± 4.31) |  |
| Category I - Baseline             | 2.76 (± 1.85)  | 2.77 (± 1.38)  | 2.94 (± 1.93)  |  |
| Category I - Change from Baseline | -0.03 (± 1.83) | -0.45 (± 1.47) | -0.32 (± 1.75) |  |
| Category J - Baseline             | 3.92 (± 3.98)  | 5.58 (± 6.05)  | 5.22 (± 4.47)  |  |
| Category J - Change from Baseline | -1.34 (± 3.64) | -0.83 (± 2.61) | -1.55 (± 4.34) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 10: Change From Baseline to 12 Week Endpoint in Conners' Teacher Rating Scale-Revised: Short Form (CTRS-R:S)

|                                                                                                                                                                                                                                                                                               |                                                                                                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                               | 10: Change From Baseline to 12 Week Endpoint in Conners' Teacher Rating Scale-Revised: Short Form (CTRS-R:S) |
| End point description:                                                                                                                                                                                                                                                                        |                                                                                                              |
| A 28-item rating scale (0 [not at all/never] to 3 [very much true/very often]) completed by the teacher to assess problem behaviors related to ADHD. Subscale total scores range from 0 to 15 for Oppositional and Cognitive Problems, 0 to 21 for Hyperactivity, and 0 to 36 for ADHD Index. |                                                                                                              |
| End point type                                                                                                                                                                                                                                                                                | Secondary                                                                                                    |
| End point timeframe:                                                                                                                                                                                                                                                                          |                                                                                                              |
| Baseline, 12 Weeks                                                                                                                                                                                                                                                                            |                                                                                                              |

| End point values                          | Pure ADHD (Period II)  | ADHD+Internalizing Disorders (Period II) | ADHD+Externalizing Disorders (Period II) |  |
|-------------------------------------------|------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                        | Reporting group        | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed               | 60                     | 15                                       | 53                                       |  |
| Units: units on a scale                   |                        |                                          |                                          |  |
| arithmetic mean (confidence interval 95%) |                        |                                          |                                          |  |
| Oppositional                              | -1.42 (-2.22 to -0.61) | 1.07 (-0.33 to 2.46)                     | -2.35 (-3.55 to -1.15)                   |  |
| Cognitive Problems                        | -1.08 (-1.72 to -0.45) | -0.47 (-1.74 to 0.8)                     | -0.94 (-1.77 to -0.11)                   |  |
| Hyperactivity                             | -2.87 (-4.04 to -1.69) | -2.34 (-4.8 to 0.11)                     | -4.09 (-5.52 to -2.67)                   |  |
| ADHD Index                                | -4.96 (-6.36 to -3.52) | -3.6 (-6.65 to 0.55)                     | -6.62 (-8.59 to -4.65)                   |  |

## **Statistical analyses**

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

B4Z-IT-LYDS

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Pure ADHD |
|-----------------------|-----------|

Reporting group description: -

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | ADHD plus internalizing disorders |
|-----------------------|-----------------------------------|

Reporting group description: -

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | ADHD plus externalizing disorders |
|-----------------------|-----------------------------------|

Reporting group description: -

| Serious adverse events                               | Pure ADHD      | ADHD plus internalizing disorders | ADHD plus externalizing disorders |
|------------------------------------------------------|----------------|-----------------------------------|-----------------------------------|
| Total subjects affected by serious adverse events    |                |                                   |                                   |
| subjects affected / exposed                          | 1 / 97 (1.03%) | 0 / 38 (0.00%)                    | 2 / 128 (1.56%)                   |
| number of deaths (all causes)                        | 0              | 0                                 | 0                                 |
| number of deaths resulting from adverse events       | 0              | 0                                 | 0                                 |
| Injury, poisoning and procedural complications       |                |                                   |                                   |
| facial bones fracture                                |                |                                   |                                   |
| alternative dictionary used: MedDRA 12.0             |                |                                   |                                   |
| subjects affected / exposed                          | 0 / 97 (0.00%) | 0 / 38 (0.00%)                    | 1 / 128 (0.78%)                   |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0                             | 0 / 1                             |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0                             | 0 / 0                             |
| fall                                                 |                |                                   |                                   |
| alternative dictionary used: MedDRA 12.0             |                |                                   |                                   |
| subjects affected / exposed                          | 0 / 97 (0.00%) | 0 / 38 (0.00%)                    | 1 / 128 (0.78%)                   |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0                             | 0 / 1                             |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0                             | 0 / 0                             |
| General disorders and administration site conditions |                |                                   |                                   |
| idiosyncratic drug reaction                          |                |                                   |                                   |



|                                                    |                |                |                 |
|----------------------------------------------------|----------------|----------------|-----------------|
| alternative dictionary used:<br>MedDRA 12.0        |                |                |                 |
| subjects affected / exposed                        | 0 / 97 (0.00%) | 0 / 38 (0.00%) | 1 / 128 (0.78%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                         |                |                |                 |
| vomiting                                           |                |                |                 |
| alternative dictionary used:<br>MedDRA 12.0        |                |                |                 |
| subjects affected / exposed                        | 0 / 97 (0.00%) | 0 / 38 (0.00%) | 1 / 128 (0.78%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                        |                |                |                 |
| appendicitis                                       |                |                |                 |
| alternative dictionary used:<br>MedDRA 12.0        |                |                |                 |
| subjects affected / exposed                        | 1 / 97 (1.03%) | 0 / 38 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Metabolism and nutrition disorders                 |                |                |                 |
| dehydration                                        |                |                |                 |
| alternative dictionary used:<br>MedDRA 12.0        |                |                |                 |
| subjects affected / exposed                        | 0 / 97 (0.00%) | 0 / 38 (0.00%) | 1 / 128 (0.78%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

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

| <b>Non-serious adverse events</b>                        | Pure ADHD        | ADHD plus<br>internalizing<br>disorders | ADHD plus<br>externalizing<br>disorders |
|----------------------------------------------------------|------------------|-----------------------------------------|-----------------------------------------|
| Total subjects affected by non-serious<br>adverse events |                  |                                         |                                         |
| subjects affected / exposed                              | 70 / 97 (72.16%) | 28 / 38 (73.68%)                        | 87 / 128 (67.97%)                       |
| Investigations                                           |                  |                                         |                                         |
| weight decreased                                         |                  |                                         |                                         |
| alternative dictionary used:<br>MedDRA 12.0              |                  |                                         |                                         |
| subjects affected / exposed                              | 11 / 97 (11.34%) | 1 / 38 (2.63%)                          | 12 / 128 (9.38%)                        |
| occurrences (all)                                        | 15               | 1                                       | 15                                      |
| Nervous system disorders                                 |                  |                                         |                                         |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                             |                                                                                                                               |                                                                                                                                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| <p>headache</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <p>20 / 97 (20.62%)</p> <p>34</p>                                                                                           | <p>10 / 38 (26.32%)</p> <p>17</p>                                                                                             | <p>26 / 128 (20.31%)</p> <p>35</p>                                                                                                |
| <p>somnolence</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <p>22 / 97 (22.68%)</p> <p>23</p>                                                                                           | <p>11 / 38 (28.95%)</p> <p>15</p>                                                                                             | <p>34 / 128 (26.56%)</p> <p>44</p>                                                                                                |
| <p>General disorders and administration site conditions</p> <p>asthenia</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>fatigue</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>irritability</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 97 (5.15%)</p> <p>6</p> <p>5 / 97 (5.15%)</p> <p>5</p> <p>4 / 97 (4.12%)</p> <p>4</p> <p>3 / 97 (3.09%)</p> <p>3</p> | <p>6 / 38 (15.79%)</p> <p>6</p> <p>0 / 38 (0.00%)</p> <p>0</p> <p>6 / 38 (15.79%)</p> <p>6</p> <p>0 / 38 (0.00%)</p> <p>0</p> | <p>7 / 128 (5.47%)</p> <p>7</p> <p>2 / 128 (1.56%)</p> <p>3</p> <p>12 / 128 (9.38%)</p> <p>16</p> <p>8 / 128 (6.25%)</p> <p>8</p> |
| <p>Gastrointestinal disorders</p> <p>abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain upper</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>constipation</p>                                                                                                                                                                                                                                                       | <p>9 / 97 (9.28%)</p> <p>13</p> <p>5 / 97 (5.15%)</p> <p>5</p>                                                              | <p>8 / 38 (21.05%)</p> <p>9</p> <p>6 / 38 (15.79%)</p> <p>8</p>                                                               | <p>18 / 128 (14.06%)</p> <p>32</p> <p>12 / 128 (9.38%)</p> <p>17</p>                                                              |

|                                                                                                                                                                                     |                                   |                                   |                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------------|------------------------------------|
| <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                     | <p>2 / 97 (2.06%)</p> <p>2</p>    | <p>2 / 38 (5.26%)</p> <p>2</p>    | <p>1 / 128 (0.78%)</p> <p>1</p>    |
| <p>diarrhoea</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                    | <p>1 / 97 (1.03%)</p> <p>3</p>    | <p>2 / 38 (5.26%)</p> <p>2</p>    | <p>3 / 128 (2.34%)</p> <p>3</p>    |
| <p>nausea</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                       | <p>12 / 97 (12.37%)</p> <p>17</p> | <p>10 / 38 (26.32%)</p> <p>19</p> | <p>26 / 128 (20.31%)</p> <p>36</p> |
| <p>vomiting</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                     | <p>13 / 97 (13.40%)</p> <p>23</p> | <p>6 / 38 (15.79%)</p> <p>13</p>  | <p>15 / 128 (11.72%)</p> <p>20</p> |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 97 (3.09%)</p> <p>3</p>    | <p>0 / 38 (0.00%)</p> <p>0</p>    | <p>8 / 128 (6.25%)</p> <p>10</p>   |
| <p>Psychiatric disorders</p> <p>aggression</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                      | <p>4 / 97 (4.12%)</p> <p>5</p>    | <p>1 / 38 (2.63%)</p> <p>1</p>    | <p>9 / 128 (7.03%)</p> <p>9</p>    |
| <p>Infections and infestations</p> <p>gastroenteritis</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>           | <p>2 / 97 (2.06%)</p> <p>2</p>    | <p>2 / 38 (5.26%)</p> <p>2</p>    | <p>0 / 128 (0.00%)</p> <p>0</p>    |
| <p>Metabolism and nutrition disorders</p> <p>anorexia</p> <p>alternative dictionary used:<br/>MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>           | <p>24 / 97 (24.74%)</p> <p>26</p> | <p>11 / 38 (28.95%)</p> <p>15</p> | <p>33 / 128 (25.78%)</p> <p>39</p> |

|                                             |                  |                 |                   |
|---------------------------------------------|------------------|-----------------|-------------------|
| decreased appetite                          |                  |                 |                   |
| alternative dictionary used:<br>MedDRA 12.0 |                  |                 |                   |
| subjects affected / exposed                 | 11 / 97 (11.34%) | 7 / 38 (18.42%) | 14 / 128 (10.94%) |
| occurrences (all)                           | 13               | 7               | 20                |

## 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

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

|                                                                                                                                                                                                                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The original intent was to also calculate change and 95% confidence intervals at end of Period III; however, due to low number of patients completing Period III, variations from baseline (LOCF), are not suitable for further analysis or description. |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Notes: