



Clinical trial results:

A Long-term, Multicenter, Open-label Trial to Evaluate the Safety and Tolerability of Flexible-Dose Brexpiprazole as Maintenance Treatment in Adolescents (13-17 Years Old) With Schizophrenia

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2017-001459-30 |
| Trial protocol | HU ES PL BG FR IT RO |
| Global end of trial date | 22 April 2025 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 31 October 2025 |
| First version publication date | 31 October 2025 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 331-10-236 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03238326 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Otsuka Pharmaceutical Development & Commercialization, Inc. |
| Sponsor organisation address | 2440 Research Blvd, Rockville, MD, United States, 20850 |
| Public contact | Clinical Transparency, Otsuka Pharmaceutical Development & Commercialization, Inc., +1 8446878522, clinicaltransparency@otsuka-us.com |
| Scientific contact | Clinical Transparency, Otsuka Pharmaceutical Development & Commercialization, Inc., +1 8446878522, clinicaltransparency@otsuka-us.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000001-PIP00-00 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 22 April 2025 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 April 2025 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to learn about the safety and tolerability of brexpiprazole as maintenance treatment in adolescents with schizophrenia.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 23 August 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | United States: 34 |
| Country: Number of subjects enrolled | Mexico: 81 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | Serbia: 28 |
| Country: Number of subjects enrolled | Ukraine: 96 |
| Country: Number of subjects enrolled | Poland: 9 |
| Country: Number of subjects enrolled | Romania: 16 |
| Country: Number of subjects enrolled | Italy: 3 |
| Country: Number of subjects enrolled | Russian Federation: 26 |
| Country: Number of subjects enrolled | France: 1 |
| Worldwide total number of subjects | 295 |
| EEA total number of subjects | 30 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 279 |
| Adults (18-64 years) | 16 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at multiple sites globally from 23 August 2017 to 22 April 2025. 14 subjects underwent a cross-titration and received brexpiprazole for up to 4 weeks in conversion period followed by subsequent enrollment in De-Novo open label treatment (OLT) period.

Pre-assignment

Screening details:

Of the 295 subjects who were enrolled for the study, 294 subjects received the study treatment, and 1 subject did not receive the study drug. All eligible subjects who rolled over from the previous study 331-10-234 (NCT03198078), and de novo subjects received brexpiprazole tablets during this study.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Open-label Period (About 25 months) (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

NA

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Prior & Current Brexpiprazole (OLT Period) |

Arm description:

Subjects who received brexpiprazole in the previous study 331-10-234 were administered brexpiprazole tablets, orally, once a day (QD) at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days. Open-label Treatment Period = OLT Period.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Brexpiprazole |
| Investigational medicinal product code | |
| Other name | OPC-34712 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

0.5, 1, 2, 3, or 4 mg/day

| | |
|------------------|---|
| Arm title | Prior Aripiprazole & Current Brexpiprazole (OLT Period) |
|------------------|---|

Arm description:

Subjects who received aripiprazole in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

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

| | |
|---|--|
| Investigational medicinal product name | Brexpiprazole |
| Investigational medicinal product code | |
| Other name | OPC-34712 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: 0.5, 1, 2, 3, or 4 mg/day | |
| Arm title | Prior Placebo & Current Brexpiprazole (OLT Period) |

Arm description:

Subjects who received brexpiprazole or aripiprazole matching placebo tablets in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|---|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Brexpiprazole |
| Investigational medicinal product code | |
| Other name | OPC-34712 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: 0.5, 1, 2, 3, or 4 mg/day | |
| Arm title | De Novo (OLT Period) |

Arm description:

De novo subjects who rolled over from the previous study 331-10-234, and newly enrolled subjects in this study were administered brexpiprazole tablets, orally, QD, at a starting dose of 0.5 mg/day from Day 1 to Day 4. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Brexpiprazole |
| Investigational medicinal product code | |
| Other name | OPC-34712 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

0.5, 1, 2, 3, or 4 mg/day

| Number of subjects in period 1 | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) |
|--------------------------------|--|---|--|
| | | | |
| Started | 99 | 89 | 87 |
| Completed | 58 | 59 | 50 |
| Not completed | 41 | 30 | 37 |
| Consent withdrawn by subject | 14 | 8 | 11 |
| Physician decision | - | 2 | - |

| | | | |
|--------------------------------|----|---|----|
| Adverse event, non-fatal | 4 | 2 | 3 |
| Reason Not Specified | 2 | 3 | 4 |
| Non-Compliance With Study Drug | 1 | 1 | 1 |
| Pregnancy | 1 | 1 | - |
| Lost to follow-up | 5 | 6 | 3 |
| Withdrawal by Caregiver | 10 | 5 | 11 |
| Lack of efficacy | 4 | 2 | 1 |
| Protocol deviation | - | - | 3 |

| Number of subjects in period 1 | De Novo (OLT Period) |
|---------------------------------------|----------------------|
| Started | 20 |
| Completed | 11 |
| Not completed | 9 |
| Consent withdrawn by subject | 4 |
| Physician decision | - |
| Adverse event, non-fatal | - |
| Reason Not Specified | 1 |
| Non-Compliance With Study Drug | - |
| Pregnancy | - |
| Lost to follow-up | 3 |
| Withdrawal by Caregiver | 1 |
| Lack of efficacy | - |
| Protocol deviation | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Prior & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole in the previous study 331-10-234 were administered brexpiprazole tablets, orally, once a day (QD) at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days. Open-label Treatment Period = OLT Period.

| | |
|-----------------------|---|
| Reporting group title | Prior Aripiprazole & Current Brexpiprazole (OLT Period) |
|-----------------------|---|

Reporting group description:

Subjects who received aripiprazole in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|--|
| Reporting group title | Prior Placebo & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole or aripiprazole matching placebo tablets in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|----------------------|
| Reporting group title | De Novo (OLT Period) |
|-----------------------|----------------------|

Reporting group description:

De novo subjects who rolled over from the previous study 331-10-234, and newly enrolled subjects in this study were administered brexpiprazole tablets, orally, QD, at a starting dose of 0.5 mg/day from Day 1 to Day 4. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| Reporting group values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) |
|------------------------|--|---|--|
| Number of subjects | 99 | 89 | 87 |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|---------------------|-------|-------|-------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 15.5 | 15.5 | 15.4 |
| standard deviation | ± 1.6 | ± 1.4 | ± 1.5 |
| Gender categorical | | | |
| Units: participants | | | |
| Female | 53 | 49 | 42 |
| Male | 46 | 40 | 45 |

| | | | |
|--|----|----|----|
| Race/Ethnicity, Customized Units: Subjects | | | |
| Race White | 65 | 64 | 58 |
| Race Black or African American | 6 | 2 | 3 |
| Race American Indian or Alaska Native | 2 | 1 | 4 |
| Race Asian | 1 | 1 | 0 |
| Race Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Race Other | 25 | 21 | 21 |
| Race Missing | 0 | 0 | 1 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Ethnicity Hispanic or Latino | 29 | 25 | 30 |
| Ethnicity Not Hispanic or Latino | 69 | 64 | 55 |
| Ethnicity Other | 1 | 0 | 1 |
| Ethnicity Unknown | 0 | 0 | 0 |
| Ethnicity Missing | 0 | 0 | 1 |

| | | | |
|------------------------------------|----------------------|-------|--|
| Reporting group values | De Novo (OLT Period) | Total | |
| Number of subjects | 20 | 295 | |
| Age Categorical Units: Subjects | | | |

| | | | |
|--|-------|-----|--|
| Age continuous Units: years | | | |
| arithmetic mean | 15.5 | | |
| standard deviation | ± 1.0 | - | |
| Gender categorical Units: participants | | | |
| Female | 9 | 153 | |
| Male | 11 | 142 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Race White | 18 | 205 | |
| Race Black or African American | 1 | 12 | |
| Race American Indian or Alaska Native | 0 | 7 | |
| Race Asian | 0 | 2 | |
| Race Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Race Other | 1 | 68 | |
| Race Missing | 0 | 1 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Ethnicity Hispanic or Latino | 1 | 85 | |
| Ethnicity Not Hispanic or Latino | 19 | 207 | |
| Ethnicity Other | 0 | 2 | |
| Ethnicity Unknown | 0 | 0 | |
| Ethnicity Missing | 0 | 1 | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Prior & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole in the previous study 331-10-234 were administered brexpiprazole tablets, orally, once a day (QD) at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days. Open-label Treatment Period = OLT Period.

| | |
|-----------------------|---|
| Reporting group title | Prior Aripiprazole & Current Brexpiprazole (OLT Period) |
|-----------------------|---|

Reporting group description:

Subjects who received aripiprazole in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|--|
| Reporting group title | Prior Placebo & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole or aripiprazole matching placebo tablets in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|----------------------|
| Reporting group title | De Novo (OLT Period) |
|-----------------------|----------------------|

Reporting group description:

De novo subjects who rolled over from the previous study 331-10-234, and newly enrolled subjects in this study were administered brexpiprazole tablets, orally, QD, at a starting dose of 0.5 mg/day from Day 1 to Day 4. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | De Novo (Conversion Period) |
|----------------------------|-----------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Subjects underwent a cross-titration to oral brexpiprazole 1, 2, or 3 mg/day for 1 to 4 weeks to achieve the required washout of prohibited medications during the conversion period.

Primary: Number of Subjects With Adverse Events (AEs)

| | |
|-----------------|---|
| End point title | Number of Subjects With Adverse Events (AEs) ^[1] |
|-----------------|---|

End point description:

An AE is defined as any untoward medical occurrence in a clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with the study treatment.

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

End point timeframe:

From the first dose of study drug (including the conversion period and the open-label treatment period in the current study) up to 21 days after the last dose of study drug (up to approximately 25.6 months).

Notes:

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

Justification: No formal statistical hypotheses were tested for the primary end point.

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | 58 | 54 | 63 | 13 |

| End point values | De Novo (Conversion Period) | | | |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 | | | |
| Units: subjects | 5 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Serious Treatment Emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Number of Subjects With Serious Treatment Emergent Adverse Events (TEAEs) ^[2] |
|-----------------|--|

End point description:

An AE is defined as any untoward medical occurrence in a clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with the study treatment. A serious adverse event (SAE) is any AE occurring at any dose that results in death, life-threatening experience, persistent or significant disability/incapacity, in-patient hospitalization or prolongs hospitalization or congenital anomaly/birth defect. A serious TEAE is defined as an AE that occurred or worsened after the first dose of study treatment up until 30 days after the last dose. The safety population included all enrolled subjects who received at least one dose of the study drug. Subjects with conversion were analysed separately in addition to their analysis in treatment period arms.

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

End point timeframe:

From the first dose of study drug (including the conversion period and the open-label treatment period in the current study) up to 21 days after the last dose of study drug (up to approximately 25.6 months).

Notes:

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

Justification: No formal statistical hypotheses were tested for the primary end point.

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | 4 | 1 | 3 | 1 |

| End point values | De Novo (Conversion Period) | | | |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 | | | |
| Units: subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects who Discontinued the Trial due to AEs

| | |
|-----------------|---|
| End point title | Number of Subjects who Discontinued the Trial due to AEs ^[3] |
|-----------------|---|

End point description:

An AE is defined as any untoward medical occurrence in a clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with the study treatment. Subjects who discontinued the trial due to AEs were recorded. The safety population included all enrolled subjects who received at least one dose of the study drug. Subjects with conversion were analysed separately in addition to their analysis in treatment period arms.

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

End point timeframe:

From the first dose of study drug (including the conversion period and the open-label treatment period in the current study) up to 21 days after the last dose of study drug (up to approximately 25.6 months).

Notes:

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

Justification: No formal statistical hypotheses were tested for the primary end point.

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | 4 | 2 | 3 | 0 |

| End point values | De Novo (Conversion Period) | | | |
|------------------|-----------------------------------|--|--|--|
|------------------|-----------------------------------|--|--|--|

| | | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 | | | |
| Units: subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Units per Liter)

| | |
|--|--|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Units per Liter) |
| End point description: Clinical laboratory assessments included clinical chemistry (alanine aminotransferase [ALT], alkaline phosphatase, aspartate aminotransferase [AST], creatinine phosphokinase (CPK), gamma glutamyl transferase, lactate dehydrogenase. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. The data for this outcome measure was planned to be collected for only OLT period arm groups. | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: units per liter (U/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALT (n=91,85,85,20) | 0.02 (± 15.35) | 2.09 (± 10.91) | 0.60 (± 10.83) | -2.30 (± 15.13) |
| AST (n=91,84,85,20) | -0.43 (± 7.20) | 0.12 (± 8.62) | -0.92 (± 6.69) | -1.10 (± 8.35) |
| Alkaline Phosphatase (n=92,85,85,20) | -25.14 (± 59.48) | -22.36 (± 60.45) | -13.94 (± 50.63) | -28.45 (± 58.93) |
| CPK, Total (n=91,85,85,20) | -7.12 (± 114.70) | -17.98 (± 182.22) | -10.62 (± 126.12) | -69.70 (± 283.72) |
| Lactate Dehydrogenase (n=84,77,83,19) | -1.02 (± 31.03) | 0.43 (± 29.70) | -1.75 (± 26.13) | -6.05 (± 24.05) |
| Gamma Glutamyl Transferase (n=92,85,85,20) | 0.41 (± 5.97) | 1.21 (± 12.73) | 2.22 (± 13.01) | -0.35 (± 12.91) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Milligrams per Deciliter)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Milligrams per Deciliter) |
|-----------------|---|

End point description:

Clinical laboratory assessments included clinical chemistry (bilirubin, urea nitrogen, calcium, glucose, cholesterol including low-density lipoprotein (LDL-C), creatinine, Triglycerides [TG]). 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|---|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: milligrams per deciliter (mg/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Bilirubin (n=84,80,78,20) | 0.04 (± 0.27) | 0.02 (± 0.25) | -0.05 (± 0.25) | -0.02 (± 0.48) |
| Calcium (n=92,85,85,20) | -0.07 (± 0.46) | -0.16 (± 0.45) | -0.10 (± 0.34) | 0.00 (± 0.39) |
| Glucose, Fasting (n=85,84,81,19) | -0.12 (± 13.67) | 0.32 (± 11.32) | 3.11 (± 16.61) | -2.05 (± 15.11) |
| LDL-C, Fasting (n=85,83,79,19) | 0.46 (± 27.13) | 7.51 (± 25.31) | 6.20 (± 21.44) | 10.11 (± 30.02) |
| Cholesterol, Fasting (n=87,84,81,19) | 2.68 (± 32.91) | 8.69 (± 29.84) | 8.88 (± 28.02) | 16.89 (± 35.93) |
| TG, Fasting (n=87,84,81,19) | 11.46 (± 51.00) | 1.32 (± 57.12) | 2.84 (± 56.16) | 5.21 (± 42.45) |
| Creatinine (n=92,85,85,20) | 0.04 (± 0.14) | 0.02 (± 0.14) | 0.03 (± 0.12) | 0.00 (± 0.12) |
| Urea Nitrogen (n=92,85,85,20) | 0.50 (± 3.57) | 0.72 (± 3.99) | 0.25 (± 4.85) | 0.60 (± 4.10) |
| Glucose, Urine (n=94,86,85,20) | -0.01 (± 0.10) | 0.00 (± 0.00) | 0.00 (± 0.08) | 0.00 (± 0.00) |
| Protein, Urine (n=94,86,85,20) | 0.02 (± 0.49) | -0.13 (± 0.45) | -0.02 (± 0.37) | -0.05 (± 0.32) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Percentage)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Percentage) |
|-----------------|---|

End point description:

Clinical laboratory assessments of HbA1c are reported in this outcome measure. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: percentage (%) of HbA1c | | | | |
| arithmetic mean (standard deviation) | | | | |
| HbA1c (n=91,83,85,20) | 0.01 (± 0.30) | -0.01 (± 0.32) | 0.05 (± 0.45) | -0.05 (± 0.26) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Millions per Microliter)

| | |
|--|--|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Millions per Microliter) |
| End point description: | |
| Clinical laboratory assessments included hematology including the red blood cell count (RBC Count). 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. | |
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: millions/microliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| RBC Count (n=86,80,80,20) | 0.09 (± 0.36) | 0.06 (± 0.29) | 0.06 (± 0.33) | 0.01 (± 0.31) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Clinical Laboratory Tests (Parameters Assessed in Thousands per Microliter)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline in Clinical Laboratory Tests (Parameters Assessed in Thousands per Microliter) |
|-----------------|--|

End point description:

Clinical laboratory assessments included hematology (basophils, eosinophils, neutrophils, leukocytes, lymphocytes, white blood cell (WBC) count, platelets). 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: thousands per microliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Basophils (n=86,80,80,20) | 0.00 (± 0.05) | -0.01 (± 0.05) | -0.01 (± 0.05) | 0.01 (± 0.02) |
| Eosinophils (n=86,80,80,20) | 0.02 (± 0.13) | 0.02 (± 0.11) | -0.01 (± 0.12) | 0.04 (± 0.14) |
| Lymphocytes (n=86,80,80,20) | 0.07 (± 0.58) | -0.11 (± 0.62) | -0.13 (± 0.58) | 0.02 (± 0.63) |
| Neutrophils (n=86,80,80,20) | -0.18 (± 1.39) | 0.00 (± 1.48) | -0.05 (± 1.79) | -0.44 (± 1.32) |
| WBC (n=86,80,80,20) | -0.08 (± 1.53) | -0.09 (± 1.87) | -0.22 (± 1.99) | -0.35 (± 1.35) |
| Platelets (n=85,80,80,20) | -2.67 (± 59.28) | -11.01 (± 43.48) | -5.05 (± 56.07) | 19.20 (± 55.50) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters That Were Unitless)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters That Were Unitless) |
|-----------------|---|

End point description:

Clinical laboratory assessments of pH are reported in this outcome measure. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: unitless | | | | |
| arithmetic mean (standard deviation) | | | | |
| pH (n=94,86,85,20) | 0.04 (± 0.63) | -0.06 (± 0.51) | 0.03 (± 0.60) | 0.05 (± 0.69) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Milliequivalents per Liter)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Milliequivalents per Liter) |
|-----------------|---|

End point description:

Clinical laboratory assessments including chloride and potassium are reported in this outcome measure. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: milliequivalents per liter (mEq/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Chloride (n=92,85,85,20) | 0.16 (± 2.56) | -0.35 (± 2.77) | 0.19 (± 3.18) | 0.45 (± 3.59) |
| Potassium (n=92,85,85,20) | 0.02 (± 0.36) | -0.09 (± 0.46) | 0.02 (± 0.45) | 0.04 (± 0.37) |

Statistical analyses

Secondary: Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Nanograms per Milliliter)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Laboratory Tests (Parameters Assessed in Nanograms per Milliliter) |
|-----------------|---|

End point description:

Clinical laboratory assessments included prolactin for both males and females. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|---|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: nanograms per milliliter (ng/ml) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Prolactin - Females (n=50,47,41,8) | -8.34 (± 15.27) | 9.86 (± 10.24) | 6.07 (± 21.14) | -1.73 (± 9.41) |
| Prolactin - Males (n=43,38,44,11) | 0.83 (± 12.56) | 7.70 (± 8.82) | 2.42 (± 12.86) | -0.79 (± 23.91) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Clinical Laboratory Tests

| | |
|-----------------|---|
| End point title | Number of Subjects With Clinically Significant Abnormalities in Clinical Laboratory Tests |
|-----------------|---|

End point description:

Laboratory assessments included hematology, chemistry, and urinalysis. Abnormality criteria included: In mg/dL [high bilirubin ≥ 2.0 , low calcium ≤ 8.2 , high cholesterol fasting ≥ 240 , HDL-C, Fasting < 40 male (M)/ < 50 female (F); LDL-C, fasting ≥ 160 , high glucose, fasting ≥ 100 , non-fasting ≥ 200 high TG, fasting ≥ 150 , high urate ≥ 8.5 F/ ≥ 10.5 M, high protein urine ≥ 2 units increase]; high creatine kinase (units per liter [U/L]) $> 3 \times$ upper limit of normal (ULN)]; high eosinophils/leukocytes $\geq 10\%$; ALT $> 3 \times$ ULN; in mEq/L [Cl ≤ 90 ; potassium ≤ 2.5 ; sodium low ≤ 126 , high ≥ 156]; platelets $\leq 75000/\text{mm}^3$; hemoglobin $\leq 11\text{g/dL}$ M/ ≤ 9.5 F; glucose, urine ≥ 2 units inc.; casts ≥ 2 units inc.; hematocrit $\leq 37\%$ and decrease of $\geq 3\%$ points, M/ $\leq 32\%$ and $\geq 3\%$ points dec., F. Number of subjects and categories with at least 1 participant with clinically significant abnormalities were reported as per criteria defined in protocol. 'Subjects analysed' = unique subjects who were evaluated for this outcome measure. 'n' = number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--|---|--|---|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| ALT: High (n=95,87,85,20) | 1 | 1 | 0 | 1 |
| Bilirubin:High (n=92,86,85,20) | 2 | 0 | 0 | 0 |
| Calcium: Low (n=95,87,85,20) | 1 | 3 | 0 | 0 |
| Chloride: Low (n=95,87,85,20) | 1 | 0 | 1 | 0 |
| Cholesterol, Fasting :High (n=94,87,83,19) | 2 | 1 | 5 | 3 |
| Creatine Kinase :High (n=95,87,85,20) | 8 | 9 | 4 | 0 |
| Glucose, Fasting: High (n=94,87,83,19) | 29 | 26 | 18 | 9 |
| HDL Cholesterol, Fasting: Low (n=94,87,83,19) | 25 | 21 | 17 | 2 |
| LDL-C, Fasting:High (n=94,87,83,19) | 3 | 0 | 3 | 2 |
| Potassium:Low (n=95,87,85,20) | 1 | 0 | 0 | 0 |
| Sodium: Low (n=95,87,85,20) | 0 | 0 | 1 | 0 |
| Sodium: High (n=95,87,85,20) | 1 | 0 | 0 | 0 |
| TG,Fasting:High (n=94,87,83,19) | 21 | 23 | 20 | 5 |
| Urate: High (n=95,87,85,20) | 1 | 0 | 0 | 0 |
| Eosinophils/Leukocytes):High (n=94,86,85,20) | 0 | 2 | 1 | 0 |
| Hematocrit: Low (n=91,86,84,20) | 2 | 3 | 2 | 0 |
| Hemoglobin: Low (n=94,86,85,20) | 1 | 4 | 3 | 0 |
| Platelets: Low (n=94,86,85,20) | 1 | 0 | 0 | 0 |
| Glucose, Urine: High(n=95,87,85,20) | 2 | 0 | 1 | 0 |
| Protein, Urine: High(n=95,87,85,20) | 1 | 0 | 1 | 0 |
| Prolactin: High (n=95,87,85,20) | 23 | 29 | 27 | 8 |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Beats per Minute)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Beats per Minute) |
|-----------------|--|

End point description:

Vital sign measurements included pulse rate assessed in beats per minute in standing and supine position.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: beats per minute (beats/min) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pulse Rate: Standing | -0.6 (± 12.8) | -1.9 (± 10.0) | -0.5 (± 10.6) | -2.8 (± 11.0) |
| Pulse Rate: Supine | 1.1 (± 10.2) | -1.6 (± 10.1) | -0.5 (± 14.5) | 0.7 (± 11.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Millimeters of Mercury)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Millimeters of Mercury) |
|-----------------|--|

End point description:

Vital sign measurements included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Blood pressure measurements were made in the supine and standing positions after the participant has been in each position at least 3 minutes. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| SBP: Standing | 0.7 (± 9.0) | 0.5 (± 9.6) | 1.5 (± 10.8) | -1.7 (± 6.5) |
| SBP: Supine | 0.7 (± 8.9) | 0.4 (± 9.5) | 2.1 (± 11.5) | -0.3 (± 6.8) |
| DBP: Standing | 0.2 (± 7.7) | 1.2 (± 8.5) | 0.2 (± 8.3) | 0.1 (± 6.7) |
| DBP: Supine | 0.8 (± 8.5) | 0.4 (± 7.4) | -0.5 (± 7.5) | 0.4 (± 8.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Centimeters)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Centimeters) |
|-----------------|---|

End point description:

Vital sign measurements included height assessed in centimeters. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: centimeters (cm) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Height (n=93,80,84,20) | 1.4 (± 5.4) | 2.4 (± 4.5) | 2.0 (± 4.2) | 3.5 (± 4.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Kilograms)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Kilograms) |
|-----------------|---|

End point description:

Vital sign measurements included weight assessed in kilograms. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Weight | 3.8 (± 5.8) | 4.2 (± 7.5) | 3.8 (± 6.6) | 3.4 (± 4.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Celsius)

| | |
|---|---|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Celsius) |
| End point description: Vital sign measurements included temperature assessed in celsius. The data for this outcome measure was planned to be collected for only OLT period arm groups. | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: celsius (°C) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Temperature | -0.0 (± 0.4) | -0.0 (± 0.3) | -0.0 (± 0.4) | 0.0 (± 0.3) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Z-Score)

| | |
|--|---|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Z-Score) |
| End point description: Vital sign measurements included Z-score for body weight, height, and BMI. To adjust for normal growth, z-scores were derived, which normalize for the natural growth of pediatric patients and adolescents by comparisons to age- and gender-matched population standards. Z-score was calculated as the deviation of the subject's each parameter from the mean for the respective parameter of the reference population divided by the standard deviation (SD) for the reference population. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: z-score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Z-Score of Body Weight | -0.0 (± 0.5) | -0.0 (± 0.5) | 0.0 (± 0.5) | 0.0 (± 0.4) |
| Z-Score of Height (n=93,80,84,20) | -0.1 (± 0.8) | 0.1 (± 0.5) | 0.0 (± 0.5) | 0.3 (± 0.6) |
| Z-Score of BMI (n=93,80,84,20) | 0.0 (± 0.6) | -0.1 (± 0.6) | 0.0 (± 0.6) | -0.1 (± 0.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Vital Signs (Parameters Assessed in Kilograms per Meter Square)

| | |
|---|--|
| End point title | Mean Change From Baseline in Vital Signs (Parameters Assessed in Kilograms per Meter Square) |
| End point description: Vital sign measurements included body mass index (BMI). | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexiprazole (OLT Period) | Prior Aripiprazole & Current Brexiprazole (OLT Period) | Prior Placebo & Current Brexiprazole (OLT Period) | De Novo (OLT Period) |
|---|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: kilograms per meter square (kg/m ²) | | | | |
| arithmetic mean (standard deviation) | | | | |
| BMI (n=93,80,84,20) | 1.0 (± 2.3) | 0.9 (± 2.8) | 0.8 (± 2.2) | 0.1 (± 2.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

| | |
|--|---|
| End point title | Number of Subjects With Clinically Significant Abnormalities in Vital Signs |
| End point description: | |
| Vital sign measurements included SBP, and DBP, pulse rate, body temperature, body weight, BMI, and height. Vital sign measurements included pulse rate in supine and standing positions (low: <50 beats per minute [bpm] and decrease ≥15 bpm; High: >120 bpm and increase ≥15 bpm), SBP in supine and standing positions (low: <110 mmHg and decrease ≥20 mmHg; High: >120 mmHg and increase ≥20 mmHg), DBP in supine and standing positions (low: <60 mmHg and decrease ≥15 mmHg; High: >80 mmHg and increase ≥15 mmHg), weight in kg (low: ≥7% decrease; High: ≥7% increase), orthostatic hypotension, (≥20mmHg decrease in SBP or ≥10 mmHg in DBP in heart rate from supine to standing). Number of subjects with clinically significant abnormalities in vital signs were reported as per criteria defined in protocol. The categories with at least one participant with clinically significant abnormalities in vital signs are reported. | |
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexiprazole (OLT Period) | Prior Aripiprazole & Current Brexiprazole (OLT Period) | Prior Placebo & Current Brexiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| SBP, Standing: Low | 7 | 5 | 6 | 0 |
| SBP, Standing: High | 10 | 11 | 14 | 2 |
| SBP, Supine: Low | 9 | 7 | 5 | 0 |
| SBP, Supine: High | 3 | 8 | 9 | 0 |
| DBP, Standing: Low | 1 | 5 | 1 | 1 |
| DBP, Standing: High | 14 | 14 | 18 | 3 |
| DBP, Supine: Low | 6 | 3 | 3 | 2 |
| DBP, Supine: High | 12 | 11 | 8 | 0 |

| | | | | |
|------------------------------|----|----|----|----|
| Pulse Rate, Standing: High | 0 | 0 | 1 | 0 |
| Pulse Rate, Supine: Low | 0 | 0 | 1 | 0 |
| Pulse Rate, Supine: High | 0 | 0 | 1 | 0 |
| Weight: Low | 9 | 5 | 9 | 1 |
| Weight: High | 46 | 40 | 40 | 13 |
| Orthostatic Hypotension: Low | 16 | 23 | 12 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Electrocardiogram (ECG) (Parameters Assessed in Milliseconds)

| | |
|-----------------|--|
| End point title | Mean Change From Baseline in Electrocardiogram (ECG) (Parameters Assessed in Milliseconds) |
|-----------------|--|

End point description:

12-lead ECG recordings were obtained for parameters including PR interval, QRS duration, QT interval, QTcB [QT interval as corrected for heart rate by Bazett's formula] interval, QTcF [QT interval as corrected for heart rate by Fridericia's formula] interval, QTcN [QT interval corrected for heart rate by the FDA Neuropharm] interval, and RR interval. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: milliseconds (ms) | | | | |
| arithmetic mean (standard deviation) | | | | |
| PR Interval (n=96,86,84,20) | 4.2 (± 14.4) | 2.5 (± 14.3) | 3.6 (± 15.6) | -2.0 (± 16.2) |
| QRS Duration (n=96,86,84,20) | 1.6 (± 8.1) | 1.5 (± 7.8) | 0.8 (± 6.8) | 1.1 (± 10.1) |
| QT Interval (n=96,86,84,20) | 4.8 (± 27.9) | 5.6 (± 28.0) | 1.3 (± 26.7) | 1.6 (± 27.8) |
| QTCB Interval (n=96,86,84,20) | -0.9 (± 26.5) | -0.1 (± 25.2) | -0.8 (± 28.6) | 5.6 (± 20.5) |
| QTcF Interval (n=96,86,84,20) | 1.1 (± 19.6) | 1.8 (± 20.8) | -0.1 (± 21.9) | 4.1 (± 16.4) |
| QTCN Interval (n=96,86,84,20) | 0.7 (± 20.4) | 1.5 (± 21.2) | -0.3 (± 22.9) | 4.3 (± 16.6) |
| RR Interval (n=96,86,84,20) | 26.9 (± 175.1) | 26.5 (± 146.1) | 10.0 (± 166.0) | -12.3 (± 147.7) |

Statistical analyses

Secondary: Mean Change From Baseline in ECG Parameters (Parameters Assessed in Beats per Minute)

| | |
|-----------------|---|
| End point title | Mean Change From Baseline in ECG Parameters (Parameters Assessed in Beats per Minute) |
|-----------------|---|

End point description:

Twelve-lead ECG recordings were obtained for parameters including mean heart rate. 'Subjects analysed' indicates the unique subjects who were evaluated for this outcome measure. 'n' signifies number of subjects analysed at specific category. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: beats/min | | | | |
| arithmetic mean (standard deviation) | | | | |
| Mean Heart Rate (n=96,86,84,20) | -2.1 (± 14.7) | -1.7 (± 13.3) | -0.8 (± 13.8) | 1.8 (± 13.6) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in ECG Parameters

| | |
|-----------------|--|
| End point title | Number of Subjects With Clinically Significant Abnormalities in ECG Parameters |
|-----------------|--|

End point description:

12-lead ECG recordings were obtained for certain parameters and the 12-lead ECG abnormality criteria included bradycardia ≤ 50 bpm and decrease ≥ 15 bpm; sinus bradycardia ≤ 50 bpm and decrease of ≥ 15 bpm, supraventricular premature beat (SVPB)-not present at baseline and present post baseline, ventricular premature beat (VPB)-not present at baseline and present post baseline; and primary (1°) atrioventricular (AV) block (PR ≥ 200 milliseconds [msec] and increase of ≥ 50 msec, right bundle-branch block) and symmetrical T-wave inversion (Sym T Wave Inv) – both not present at baseline and present post baseline; Increase in QTc-QTcF ≥ 450 msec for males, ≥ 470 msec for females. Number of subjects and categories with at least 1 participant with clinically significant ECG abnormalities are reported as per the criteria defined in the protocol. 'Subjects analysed' indicates unique subjects who were evaluated for this outcome measure. 'n'=number of subjects analysed at specific category.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexipiprazole (OLT Period) | Prior Aripiprazole & Current Brexipiprazole (OLT Period) | Prior Placebo & Current Brexipiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| Bradycardia (n=96, 86, 84, 20) | 4 | 1 | 1 | 0 |
| Sinus Bradycardia (n=96, 86, 84, 20) | 4 | 1 | 1 | 0 |
| SVPB (n=96, 86, 84, 20) | 1 | 1 | 2 | 0 |
| VPB (n=95, 87, 85, 20) | 1 | 1 | 0 | 0 |
| 1° AV Block (n=96, 86, 84, 20) | 1 | 2 | 0 | 0 |
| RBBB (n=96, 87, 85, 20) | 1 | 0 | 1 | 0 |
| Sym T-Wave Inv (n=96, 87, 85, 20) | 0 | 0 | 0 | 1 |
| QT (n=96, 86, 84, 20) | 1 | 0 | 0 | 0 |
| Increase in QTcF (n=96, 86, 84, 20) | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline on the Abnormal Involuntary Movement Scale (AIMS) Total Score

| | |
|-----------------|---|
| End point title | Mean Change From Baseline on the Abnormal Involuntary Movement Scale (AIMS) Total Score |
|-----------------|---|

End point description:

The AIMS assessment consists of 12 items rating the involuntary movements: Facial and oral movements (4 items), extremity movements (2 items), and trunk movements (1 item) were observed unobtrusively while the participant is at rest and the investigator also made global judgments on the participant's dyskinesias (2 items), and dental status (2 items). Severity of each item was rated on a 5-point scale, with a score of 0 (absence of symptoms) to 4 (severe condition). Total Score is the sum of the scores of all 12 items, ranging from 0 to 48, higher scores indicate severe condition. A negative change reflects an improvement or reduction in the severity of abnormal movements.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexipiprazole (OLT Period) | Prior Aripiprazole & Current Brexipiprazole (OLT Period) | Prior Placebo & Current Brexipiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: score on a scale | | | | |

| | | | | |
|--------------------------------------|---------------------|---------------------|--------------------|---------------------|
| arithmetic mean (standard deviation) | -0.01 (\pm 0.30) | -0.06 (\pm 0.35) | 0.09 (\pm 0.68) | -0.05 (\pm 0.22) |
|--------------------------------------|---------------------|---------------------|--------------------|---------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline on the Simpson-Angus Scale (SAS) Total Score

| | |
|--|--|
| End point title | Mean Change From Baseline on the Simpson-Angus Scale (SAS) Total Score |
| End point description: The SAS consists of a list of 10 symptoms of Parkinsonism (gait, arm dropping, shoulder shaking, elbow rigidity, wrist rigidity, head rotation, glabella tap, tremor, salivation, and akathisia). Each item is rated on a 5-point scale, with a score of zero representing absence of symptoms, and a score of 4 representing a severe condition. The SAS Total Score is the sum of the scores for all 10 items, ranging from 0-40. A negative change reflects an improvement or reduction in Parkinsonism severity. | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | -0.18 (\pm 0.69) | -0.33 (\pm 0.77) | 0.17 (\pm 1.40) | -0.75 (\pm 2.38) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in the Barnes Akathisia Rating Scale (BARS) Total Score

| | |
|---|---|
| End point title | Mean Change From Baseline in the Barnes Akathisia Rating Scale (BARS) Total Score |
| End point description: The BARS score is based only on the item of "Global Clinical Assessment of Akathisia". The BARS consists of 4 items related to akathisia as follows. Item 1: objective observation of akathisia by the investigator; Item 2: subjective feelings of restlessness by the participant; Item 3: subjective distress due to akathisia; and Item 4: global clinical assessment of akathisia. The first 3 items will be rated on a 4-point Likert scale from 0 to 3, with 0 representing absence of symptoms and 3 representing a severe condition. The BARS global clinical assessment score refers to the ratings from the 4th item Global Clinical Assessment of Akathisia, which is a 6-point Likert scale from 0 to 5, with 0 representing absence | |

of symptoms and 5 representing severe akathisia. Total score is the sum of the scores of all 4 items, ranging from 0 to 14. Higher score indicates severe akathisia. A negative change from baseline reflects improvement or reduction in the severity of akathisia symptoms.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | -0.02 (± 0.29) | -0.08 (± 0.34) | 0.02 (± 0.53) | -0.15 (± 0.49) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Psychotropic Side Effects as Assessed by Udvalg for Kliniske Undersogelser (UKU) Rating Scale

| | |
|-----------------|---|
| End point title | Number of Subjects With Psychotropic Side Effects as Assessed by Udvalg for Kliniske Undersogelser (UKU) Rating Scale |
|-----------------|---|

End point description:

The UKU rating scale is a semi-structured interview used to assess the side effects of subjects being treated with antipsychotic drugs. Each item (i.e., each symptom) of the UKU side effects is defined by the means of a 4-point-scale (0-1-2-3) if it is assessed in psychic, autonomic (auto), neurologic, other categories. In general, Degree 0 means "doubtfully or not present (NP)", and Degrees 1, 2, and 3 indicate that the symptom is present to a mild, moderate or severe degree, respectively. The data for this outcome measure was planned to be collected for only OLT period arm groups.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| Psychic:Concentration Difficulties: NP | 38 | 30 | 32 | 2 |
| Psychic:Concentration Difficulties: Mild | 30 | 30 | 33 | 9 |

| | | | | |
|--|----|----|----|----|
| Psychic:Concentration Difficulties: Moderate | 29 | 24 | 20 | 8 |
| Psychic:Concentration Difficulties: Severe | 1 | 5 | 2 | 1 |
| Psychic:Asthenia/Lassitude: NP | 59 | 49 | 44 | 5 |
| Psychic:Asthenia/Lassitude: Mild | 26 | 24 | 30 | 9 |
| Psychic:Asthenia/Lassitude: Moderate | 13 | 16 | 13 | 6 |
| Psychic:Sleepiness/Sedation: NP | 77 | 65 | 63 | 9 |
| Psychic:Sleepiness/Sedation: Mild | 16 | 20 | 23 | 10 |
| Psychic: Sleepiness/Sedation: Moderate | 5 | 4 | 1 | 1 |
| Psychic: Failing Memory, Degree: NP | 56 | 51 | 49 | 9 |
| Psychic: Failing Memory: Mild | 28 | 21 | 27 | 5 |
| Psychic: Failing Memory: Moderate | 14 | 17 | 11 | 6 |
| Psychic: Depression:NP | 60 | 49 | 46 | 7 |
| Psychic: Depression: Mild | 31 | 26 | 31 | 7 |
| Psychic: Depression: Moderate | 6 | 13 | 10 | 6 |
| Psychic: Depression: Severe | 1 | 1 | 0 | 0 |
| Psychic: Tension/Lnner Unrest: NP | 46 | 37 | 35 | 5 |
| Psychic: Tension/Lnner Unrest: Mild | 36 | 32 | 35 | 13 |
| Psychic: Tension/Lnner Unrest: Moderate | 15 | 20 | 15 | 1 |
| Psychic: Tension/Lnner Unrest: Severe | 1 | 0 | 2 | 1 |
| Psychic: Increased Duration Of Sleep: NP | 82 | 79 | 73 | 13 |
| Psychic: Increased Duration Of Sleep: Mild | 16 | 7 | 12 | 6 |
| Psychic: Increased Duration Of Sleep: Moderate | 0 | 3 | 2 | 1 |
| Psychic: Reduced Duration Of Sleep, Degree: NP | 88 | 69 | 68 | 12 |
| Psychic: Reduced Duration Of Sleep: Mild | 7 | 15 | 18 | 5 |
| Psychic: Reduced Duration Of Sleep: Moderate | 2 | 5 | 1 | 3 |
| Psychic: Reduced Duration Of Sleep: Severe | 1 | 0 | 0 | 0 |
| Psychic: Inc. Dream Activity: NP | 88 | 75 | 74 | 15 |
| Psychic: Inc. Dream Activity: Mild | 10 | 11 | 11 | 5 |
| Psychic: Inc. Dream Activity: Moderate | 0 | 3 | 2 | 0 |
| Psychic: Emotional Indifference: NP | 45 | 47 | 48 | 3 |
| Psychic: Emotional Indifference: Mild | 33 | 24 | 22 | 7 |
| Psychic: Emotional Indifference: Moderate | 20 | 17 | 15 | 10 |
| Psychic: Emotional Indifference: Severe | 0 | 1 | 2 | 0 |
| Neurologic: Dystonia: NP | 94 | 88 | 85 | 20 |
| Neurologic: Dystonia: Mild | 3 | 1 | 2 | 0 |
| Neurologic: Dystonia: Moderate | 1 | 0 | 0 | 0 |
| Neurologic: Rigidity: Not Present | 94 | 87 | 81 | 17 |
| Neurologic: Rigidity: Mild | 4 | 2 | 6 | 3 |
| Neurologic: Hypokinesia/Akinesia: NP | 93 | 85 | 82 | 19 |
| Neurologic: Hypokinesia/Akinesia: Mild | 5 | 4 | 4 | 1 |
| Neurologic: Hypokinesia/Akinesia: Moderate | 0 | 0 | 1 | 0 |
| Neurologic: Hyperkinesia Logic: NP | 96 | 89 | 85 | 20 |
| Neurologic: Hyperkinesia Logic: Mild | 1 | 0 | 2 | 0 |

| | | | | |
|---|----|----|----|----|
| Neurologic: Hyperkinesia Logic: Moderate | 1 | 0 | 0 | 0 |
| Neurologic: Tremor: Not Present | 86 | 83 | 75 | 17 |
| Neurologic: Tremor: Mild | 11 | 5 | 10 | 3 |
| Neurologic: Tremor: Moderate | 1 | 1 | 2 | 0 |
| Neurologic: Akathisia: Not Present | 93 | 77 | 74 | 19 |
| Neurologic: Akathisia: Mild | 4 | 9 | 11 | 1 |
| Neurologic: Akathisia: Moderate | 1 | 3 | 2 | 0 |
| Neurologic: Epileptic Seizures: NP | 98 | 89 | 87 | 20 |
| Neurologic: Paraesthesias: NP | 98 | 87 | 85 | 20 |
| Neurologic: Paraesthesias: Mild | 0 | 2 | 2 | 0 |
| Auto:Accommodation Disturbances :NP | 98 | 87 | 85 | 16 |
| Auto:Accommodation Disturbances:Mild | 0 | 1 | 2 | 0 |
| Auto:Accommodation Disturbances:Moderate | 0 | 1 | 0 | 4 |
| Auto:Increased Salivation:Not Present | 95 | 84 | 81 | 20 |
| Auto:Increased Salivation:Mild | 3 | 4 | 3 | 0 |
| Auto:Increased Salivation:Moderate | 0 | 0 | 3 | 0 |
| Auto:Increased Salivation:Severe | 0 | 1 | 0 | 0 |
| Auto:Reduced Salivation: Not Present | 98 | 88 | 83 | 19 |
| Auto:Reduced Salivation: Mild | 0 | 1 | 4 | 1 |
| Auto:Nausea/Vomiting:Not Present | 93 | 86 | 76 | 19 |
| Auto:Nausea/Vomiting:Mild | 4 | 2 | 9 | 1 |
| Auto:Nausea/Vomiting:Moderate | 1 | 1 | 1 | 0 |
| Auto:Nausea/Vomiting:Severe | 0 | 0 | 1 | 0 |
| Auto:Diarrhoea: Not Present | 97 | 88 | 84 | 20 |
| Auto:Diarrhoea: Mild | 1 | 0 | 2 | 0 |
| Auto:Diarrhoea: Moderate | 0 | 1 | 1 | 0 |
| Auto:Constipation:Not Present | 95 | 87 | 85 | 17 |
| Auto:Constipation:Mild | 2 | 2 | 2 | 3 |
| Auto:Constipation:Moderate | 1 | 0 | 0 | 0 |
| Auto:Micturition Disturbances: NP | 97 | 88 | 85 | 20 |
| Auto:Micturition Disturbances: Mild | 1 | 1 | 1 | 0 |
| Auto:Micturition Disturbances: Moderate | 0 | 0 | 1 | 0 |
| Auto:Polyuria/Polydipsia:Not Present | 97 | 85 | 84 | 20 |
| Auto:Polyuria/Polydipsia, Degree:Mild | 0 | 4 | 1 | 0 |
| Auto:Polyuria/Polydipsia:Moderate | 1 | 0 | 2 | 0 |
| Auto:Orthostatic Dizziness: Not Present | 95 | 84 | 81 | 17 |
| Auto:Orthostatic Dizziness: Mild | 3 | 5 | 5 | 3 |
| Auto:Orthostatic Dizziness: Moderate | 0 | 0 | 1 | 0 |
| Auto:Palpitations/Tachycardia:Not Present | 94 | 85 | 82 | 17 |
| Auto:Palpitations/Tachycardia:Mild | 3 | 4 | 3 | 3 |
| Auto:Palpitations/Tachycardia:Moderate | 1 | 0 | 1 | 0 |
| Auto:Palpitations/Tachycardia:Severe | 0 | 0 | 1 | 0 |
| Auto:Inc. Tendency To Sweat:NP | 84 | 19 | 84 | 19 |
| Auto:Inc. Tendency To Sweat:Mild | 2 | 1 | 3 | 1 |
| Auto:Inc. Tendency To Sweat:Moderate | 0 | 0 | 0 | 0 |
| Auto:Inc. Tendency To Sweat:Severe | 1 | 0 | 1 | 0 |
| Other:Rash:Not Present | 98 | 89 | 87 | 20 |
| Other:Morbilliform: Mild | 2 | 0 | 0 | 0 |
| Other:Petechial: Mild | 2 | 0 | 0 | 0 |
| Other: Urticarial: Mild | 2 | 0 | 1 | 0 |

| | | | | |
|---|----|----|----|----|
| Other:Psoriatic: Mild | 2 | 0 | 0 | 0 |
| Other:Cannot Be Classified: Mild | 2 | 0 | 1 | 1 |
| Other:Pruritus, Degree: Not Present | 98 | 87 | 85 | 20 |
| Other:Pruritus: Mild | 0 | 1 | 1 | 0 |
| Other:Pruritus: Moderate | 0 | 1 | 1 | 0 |
| Other:Photosensitivity: Not Present | 97 | 86 | 86 | 20 |
| Other:Photosensitivity : Mild | 1 | 3 | 1 | 0 |
| Other:Inc. Pigmentation: NP | 98 | 89 | 87 | 20 |
| Other:Weight Gain: Not Present | 74 | 66 | 67 | 11 |
| Other:Weight Gain: Mild | 16 | 15 | 15 | 6 |
| Other:Weight Gain: Moderate | 18 | 6 | 5 | 3 |
| Other:Weight Gain: Severe | 0 | 2 | 0 | 0 |
| Other:Weight Loss: Not Present | 80 | 77 | 76 | 15 |
| Other:Weight Loss: Mild | 15 | 11 | 9 | 5 |
| Other:Weight Loss: Moderate | 3 | 1 | 2 | 0 |
| Other: Menorrhagia: NP | 70 | 64 | 61 | 16 |
| Other:Menorrhagia:Mild | 0 | 1 | 1 | 0 |
| Other:Menorrhagia:Severe | 0 | 0 | 1 | 0 |
| Other: Amenorrhoea: NP | 68 | 58 | 57 | 14 |
| Other:Amenorrhoea:Mild | 1 | 1 | 1 | 0 |
| Other:Amenorrhoea: Moderate | 0 | 1 | 0 | 0 |
| Other:Amenorrhoea:Severe | 0 | 1 | 0 | 0 |
| Other:Galactorrhoea : Not Present | 88 | 78 | 75 | 20 |
| Other:Galactorrhoea : Mild | 0 | 1 | 0 | 0 |
| Other: Gynaecomastia: NP | 77 | 70 | 70 | 17 |
| Other: Inc. Sexual Desire: Not Present | 91 | 84 | 83 | 19 |
| Other: Inc. Sexual Desire: Mild | 0 | 1 | 2 | 1 |
| Other: Inc. Sexual Desire: Moderate | 1 | 0 | 0 | 0 |
| Other:Diminished Sexual Desire: NP | 91 | 80 | 81 | 14 |
| Other:Diminished Sexual Desire: Mild | 1 | 5 | 2 | 5 |
| Other:Diminished Sexual Desire: Moderate | 0 | 0 | 2 | 0 |
| Other:Diminished Sexual Desire: Severe | 0 | 0 | 0 | 1 |
| Other:Erectile Dysfunction: NP | 66 | 53 | 63 | 10 |
| Other:Erectile Dysfunction: Mild | 0 | 3 | 0 | 2 |
| Other:Ejaculatory Dysfunction:Not Present | 65 | 54 | 62 | 12 |
| Other:Ejaculatory Dysfunction:Mild | 0 | 1 | 0 | 0 |
| Other:Ejaculatory Dysfunction:Moderate | 0 | 1 | 0 | 0 |
| Other:Orgastic Dysfunction: NP | 88 | 83 | 82 | 19 |
| Other:Orgastic Dysfunction: Mild | 0 | 1 | 1 | 1 |
| Other : Dry Vagina, Degree : Not Present | 67 | 66 | 62 | 14 |
| Other: Headache : Not Present | 98 | 89 | 87 | 20 |
| Other:Tension Headache: Mild | 2 | 4 | 5 | 3 |
| Other:Tension Headache: Moderate | 2 | 0 | 0 | 1 |
| Other:Migraine: Mild | 3 | 2 | 5 | 0 |
| Other:Other Forms: Mild | 3 | 1 | 5 | 0 |
| Other:Other Forms: Moderate | 0 | 1 | 83 | 13 |
| Other:Physical Dependence:NP | 93 | 83 | 83 | 13 |
| Other:Physical Dependence:Mild | 0 | 0 | 0 | 1 |
| Other:Physical Dependence:Moderate | 0 | 0 | 0 | 2 |
| Other:Psychic Dependence: NP | 98 | 88 | 86 | 17 |

| | | | | |
|-----------------------------------|---|---|---|---|
| Other:Psychic Dependence:Mild | 0 | 0 | 1 | 1 |
| Other:Psychic Dependence:Moderate | 0 | 0 | 0 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With At Least One Occurrence of Suicidal Behavior or Suicidal Ideation as Recorded on Columbia-Suicide Severity Rating Scale (C-SSRS)

| | |
|-----------------|--|
| End point title | Number of Subjects With At Least One Occurrence of Suicidal Behavior or Suicidal Ideation as Recorded on Columbia-Suicide Severity Rating Scale (C-SSRS) |
|-----------------|--|

End point description:

C-SSRS is a scale used to report at least one occurrence of any suicidal behavior or suicidal ideation. Suicidal behavior was defined as reporting any of the following items: actual attempt, interrupted attempt, aborted attempt, and preparatory acts or behavior. The suicidal ideation total score is the sum of intensity scores of 5 items (frequency, duration, controllability, deterrents, and reasons for ideation). The score of each intensity item ranges from 0 (none) to 5 (worst) and the total score ranges from 0 to 25. Lower scores indicate improvement. Subjects with conversion were analysed separately in addition to their analysis in treatment period arms.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | 5 | 4 | 6 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Occurrence of Cognitive Adverse Effects Assessed by New York Assessment for Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT)

| | |
|-----------------|--|
| End point title | Number of Subjects With at Least One Occurrence of Cognitive Adverse Effects Assessed by New York Assessment for Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT) |
|-----------------|--|

End point description:

The NY-AACENT is used to detect changes in cognitive function for neurological or psychiatric problems, specifically created to be used in pediatric population (ages 12 -17), but could be used with other age

groups, as appropriate. Each of the 7 items is derived from the 7 domains as follows: Working Memory, Attention/Vigilance, Verbal Learning/Memory, Visual Learning/Memory, Reasoning and Problem Solving, Speed of Processing, and Social Cognition. Each score is derived as follows: 0=not present in the past week; 1=present (during past week) and mild; 2=present (during past week) and moderate; 3=present (during past week) and severe; and 4=present (during past week) and extreme; and the item score is set to missing/unknown. The NY-AACENT total score is calculated by summing up 7 individual item scores at participant-visit level. The Total range is 0–28. Higher scores reflects greater severity and frequency of cognitive problems and lower scores shows absence or mild cognitive issues.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| Working Memory | 69 | 57 | 61 | 14 |
| Attention/Vigilance | 77 | 72 | 69 | 17 |
| Verbal Learning | 59 | 46 | 51 | 17 |
| Visual Learning | 35 | 33 | 35 | 5 |
| Reasoning | 76 | 69 | 65 | 18 |
| Speed of Processing | 72 | 59 | 59 | 15 |
| Social Cognition | 77 | 71 | 64 | 17 |
| Any Sign/Symptoms | 88 | 78 | 74 | 20 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Stages of Tanner Scale Score at Baseline and Month 24

| | |
|-----------------|---|
| End point title | Number of Subjects With Stages of Tanner Scale Score at Baseline and Month 24 |
|-----------------|---|

End point description:

The Tanner scale is a classification system used to assess physical development during puberty, detailing five distinct stages of growth. The Tanner Staging Scale assessment consists of 2 domains for girls and 3 domains for boys. Subjects with different stages in Tanner Staging Scale (Stage 1-5) Score are reported. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

Baseline, Month 24

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--|--|---|---|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 98 | 89 | 87 | 20 |
| Units: subjects | | | | |
| Boys: Baseline-Stage 1 (n=45,40,45,11) | 0 | 0 | 0 | 0 |
| Boys: Baseline-Stage 2 (n=45,40,45,11) | 4 | 3 | 0 | 0 |
| Boys: Baseline-Stage 3 (n=45,40,45,11) | 7 | 5 | 5 | 3 |
| Boys: Baseline-Stage 4 (n=45,40,45,11) | 14 | 21 | 16 | 7 |
| Boys: Baseline-Stage 5 (n=45,40,45,11) | 20 | 11 | 24 | 1 |
| Boys: Month 24-Stage 1 (n=29,28,24,6) | 0 | 0 | 0 | 0 |
| Boys: Month 24-Stage 2 (n=29,28,24,6) | 0 | 0 | 0 | 0 |
| Boys: Month 24-Stage 3 (n=29,28,24,6) | 2 | 2 | 1 | 0 |
| Boys: Month 24-Stage 4 (n=29,28,24,6) | 9 | 13 | 8 | 2 |
| Boys: Month 24-Stage 5 (n=29,28,24,6) | 18 | 13 | 15 | 4 |
| Girls: Baseline-Stage 1 (n=53,49,42,9) | 0 | 0 | 0 | 0 |
| Girls: Baseline-Stage 2 (n=53,49,42,9) | 0 | 1 | 0 | 0 |
| Girls: Baseline-Stage 3 (n=53,49,42,9) | 8 | 3 | 6 | 1 |
| Girls: Baseline-Stage 4 (n=53,49,42,9) | 17 | 21 | 16 | 8 |
| Girls: Baseline-Stage 5 (n=53,49,42,9) | 28 | 24 | 20 | 0 |
| Girls: Month 24- Stage 1 (n=27,30,27,5) | 0 | 0 | 0 | 0 |
| Girls: Month 24-Stage 2 (n=27,30,27,5) | 0 | 0 | 0 | 0 |
| Girls: Month 24-Stage 3 (n=27,30,27,5) | 0 | 0 | 0 | 0 |
| Girls: Month 24-Stage 4 (n=27,30,27,5) | 5 | 9 | 9 | 1 |
| Girls: Month 24-Stage 5 (n=27,30,27,5) | 22 | 21 | 18 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the PANSS Total Score

| | |
|--|---|
| End point title | Change From Baseline in the PANSS Total Score |
| End point description: | |
| <p>The PANSS consisted of three subscales: a total of 30 symptom constructs. For each symptom construct, severity was rated on a 7-point scale, with a score of 1 (absence of symptoms) to 7 (extremely severe symptoms). The PANSS total score was the sum of the rating scores for 7 positive (+ve) scale items, 7 negative (-ve) scale items, and 16 general psychopathology scale items from the PANSS panel. The PANSS total score ranges from 30 (best possible outcome) to 210 (worst possible outcome). Higher scores indicate worsening of symptoms. A negative change from baseline reflects improvement or reduction in symptom severity. Efficacy Sample consists of all subjects in the Safety Sample who had a baseline assessment and at least one post-baseline assessment of the PANSS Total Score. The data for this outcome measure was planned to be collected for only OLT period arm groups.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change in PANSS Total Score | -18.44 (\pm 17.53) | -20.14 (\pm 17.63) | -19.76 (\pm 18.88) | -19.00 (\pm 13.61) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the PANSS Positive Subscale Scores

| | |
|--|--|
| End point title | Change From Baseline in the PANSS Positive Subscale Scores |
| End point description: | |
| <p>The PANSS consisted of three subscales: a total of 30 symptom constructs. For each symptom construct, severity was rated on a 7-point scale, with a score of 1 (absence of symptoms) to 7 (extremely severe symptoms). The PANSS total score was the sum of the rating scores for 7 positive (+ve) scale items, 7 negative (-ve) scale items, and 16 general psychopathology scale items from the PANSS panel. The PANSS total score ranges from 30 (best possible outcome) to 210 (worst possible outcome). Higher scores indicate worsening of symptoms. A negative change from baseline reflects improvement or reduction in symptom severity. Efficacy Sample consists of all subjects in the Safety Sample who had a baseline assessment and at least one post-baseline assessment of the PANSS Total Score. The data for this outcome measure was planned to be collected for only OLT period arm groups.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change in PANSS (+ve) Subscale Score | -4.59 (\pm 5.11) | -5.20 (\pm 5.08) | -5.29 (\pm 5.75) | -5.15 (\pm 4.97) |

Statistical analyses

Secondary: Change From Baseline in the PANSS Negative Subscale Scores

| | |
|-----------------|--|
| End point title | Change From Baseline in the PANSS Negative Subscale Scores |
|-----------------|--|

End point description:

The PANSS consisted of three subscales: a total of 30 symptom constructs. For each symptom construct, severity was rated on a 7-point scale, with a score of 1 (absence of symptoms) to 7 (extremely severe symptoms). The PANSS total score was the sum of the rating scores for 7 positive scale items, 7 negative scale items, and 16 general psychopathology scale items from the PANSS panel. The PANSS total score ranges from 30 (best possible outcome) to 210 (worst possible outcome). Higher scores indicate worsening of symptoms. A negative (-ve) change from baseline reflects improvement or reduction in symptom severity. Efficacy Sample consists of all subjects in the Safety Sample who had a baseline assessment and at least one post-baseline assessment of the PANSS Total Score. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexipiprazole (OLT Period) | Prior Aripiprazole & Current Brexipiprazole (OLT Period) | Prior Placebo & Current Brexipiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change in PANSS (-ve) Subscale Score | -4.82 (± 5.46) | -4.89 (± 4.98) | -4.55 (± 5.37) | -4.40 (± 4.11) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Global Assessment Scale (CGAS) Total Score

| | |
|-----------------|---|
| End point title | Change From Baseline in Children's Global Assessment Scale (CGAS) Total Score |
|-----------------|---|

End point description:

The CGAS is a 100-point rating scale measuring psychological, social and school functioning for children aged 6-17. The scale is separated into 10-point sections with the score ranging from 0-100, 1 to 10 indicates the need for constant supervision and 91 to 100 indicates superior functioning in all areas. A positive change from baseline reflects improvement in functioning. Efficacy Sample consists of all subjects in the Safety Sample who had a baseline assessment and at least one post-baseline assessment of the PANSS Total Score. The data for this outcome measure was planned to be collected for only OLT period arm groups.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexiprazole (OLT Period) | Prior Aripiprazole & Current Brexiprazole (OLT Period) | Prior Placebo & Current Brexiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 13.58 (± 13.26) | 14.31 (± 14.13) | 12.92 (± 13.42) | 23.05 (± 12.80) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Clinical Global Impression Severity (CGI-S) Scale Score

| | |
|-----------------|--|
| End point title | Mean Clinical Global Impression Severity (CGI-S) Scale Score |
|-----------------|--|

End point description:

The CGI-S scale is an investigator-rated evaluation that assesses the severity of a participant's illness on a 7-point scale, ranging from 1 to 7. The investigator answered the following question: "Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?" Response choices include: 0 = not assessed; 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; and 7 = among the most extremely ill patients. Higher scores indicate worse condition.

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

End point timeframe:

From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24)

| End point values | Prior & Current Brexiprazole (OLT Period) | Prior Aripiprazole & Current Brexiprazole (OLT Period) | Prior Placebo & Current Brexiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|---|--|--|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | -1.09 (± 1.16) | -1.11 (± 1.20) | -0.86 (± 1.21) | -1.30 (± 1.08) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Clinical Global Impression - Improvement (CGI-I) Scale Score

| | |
|--|---|
| End point title | Mean Clinical Global Impression - Improvement (CGI-I) Scale Score |
| End point description: The efficacy of brexpiprazole in the treatment was rated for each participant using the CGI-I. The investigator rated the participant's total improvement whether or not it was entirely due to drug treatment on a 7-point scale, ranging from 0 to 7. Response choices were: 0 = not assessed, 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse. Higher scores indicate worse condition. | |
| End point type | Secondary |
| End point timeframe: From the first dose of the study drug up to the last dose in the open-label treatment period (Up to Month 24) | |

| End point values | Prior & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | Prior Placebo & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|--------------------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 87 | 85 | 20 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 2.1 (± 1.2) | 2.1 (± 1.1) | 2.2 (± 1.1) | 1.9 (± 1.1) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug (including the open-label treatment period and the conversion period in the current study) up to 21 days after the last dose of study drug (up to approximately 25.6 months)

Adverse event reporting additional description:

The safety population included all enrolled subjects who received at least one dose of the study drug. Subjects with conversion were analysed separately in addition to their analysis in treatment period arms.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | De Novo (Conversion Period) |
|-----------------------|-----------------------------|

Reporting group description:

Subjects underwent a cross-titration and received brexpiprazole tablets, orally, once a day (QD), for up to 4 weeks. The dose was increased up to 3 milligrams/day (mg/day) during cross-titration.

| | |
|-----------------------|--|
| Reporting group title | Prior & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole in the previous study 331-10-234 were administered brexpiprazole tablets, orally, once a day (QD) at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|----------------------|
| Reporting group title | De Novo (OLT Period) |
|-----------------------|----------------------|

Reporting group description:

De novo subjects who rolled over from the previous study 331-10-234, and newly enrolled subjects in this study were administered brexpiprazole tablets, orally, QD, at a starting dose of 0.5 mg/day from Day 1 to Day 4. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|--|
| Reporting group title | Prior Placebo & Current Brexpiprazole (OLT Period) |
|-----------------------|--|

Reporting group description:

Subjects who received brexpiprazole or aripiprazole matching placebo tablets in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| | |
|-----------------------|---|
| Reporting group title | Prior Aripiprazole & Current Brexpiprazole (OLT Period) |
|-----------------------|---|

Reporting group description:

Subjects who received aripiprazole in the previous study 331-10-234, were administered brexpiprazole tablets, orally, QD at a starting dose of 0.5 mg/day from Day 1 to Day 4 in this study. Thereafter, the dose was titrated to 1 mg/day by Day 7, with the option of a 1 mg increase or decrease if needed and tolerated. The dose was adjusted within the range of 1 mg/day to 2 mg/day by Day 14, 1 mg/day to 3 mg/day by Day 21, and up to a maximum of 4 mg/day by Day 22 based on clinical judgement. Subjects continued to receive flexible dose of brexpiprazole (1 mg/day to 4 mg/day) up to Month 24. Subjects were followed for safety for another 21 days.

| Serious adverse events | De Novo (Conversion Period) | Prior & Current Brexpiprazole (OLT Period) | De Novo (OLT Period) |
|---|--------------------------------|--|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 98 (4.08%) | 1 / 20 (5.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Psychomotor Hyperactivity | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Abnormal Sensations in Eye | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal Ideation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Schizophrenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic Disorder | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pilonidal Disease | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Prior Placebo & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 1 / 89 (1.12%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Psychomotor Hyperactivity | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Abnormal Sensations in Eye | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal Ideation | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schizophrenia | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 1 / 89 (1.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide Attempt | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic Disorder | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pilonidal Disease | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | De Novo (Conversion Period) | Prior & Current Brexipiprazole (OLT Period) | De Novo (OLT Period) |
|---|--------------------------------|---|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 45 / 98 (45.92%) | 13 / 20 (65.00%) |
| Investigations | | | |
| Coronavirus Test Positive | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Weight Increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 7 / 98 (7.14%) | 4 / 20 (20.00%) |
| occurrences (all) | 0 | 9 | 5 |
| Injury, poisoning and procedural complications | | | |
| Clavicle Fracture | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Akathisia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 6 / 98 (6.12%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 7 | 1 |
| Headache | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 10 / 98 (10.20%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 17 | 0 |
| Sedation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 98 (1.02%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Somnolence subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 2 | 9 / 98 (9.18%) 12 | 6 / 20 (30.00%) 7 |
| Tension Headache subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 98 (1.02%) 1 | 1 / 20 (5.00%) 1 |
| Dysarthria subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 98 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Blood and lymphatic system disorders Erythropenia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 98 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 98 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Hyperthermia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 98 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 98 (1.02%) 1 | 1 / 20 (5.00%) 1 |
| Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 98 (2.04%) 2 | 1 / 20 (5.00%) 1 |
| Cough subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 98 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Psychiatric disorders Major Depression subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 98 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Intentional Self-Injury | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 98 (1.02%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 98 (3.06%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 3 | 1 |
| Agitation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Initial Insomnia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 98 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Emotional Disorders | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 98 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 98 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Endocrine disorders | | | |
| Hyperprolactinaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle Rigidity | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 98 (4.08%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 5 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 9 / 98 (9.18%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 12 | 0 |
| Urinary Tract Infection | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 98 (3.06%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Coronavirus Pneumonia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 98 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Prior Placebo & Current Brexpiprazole (OLT Period) | Prior Aripiprazole & Current Brexpiprazole (OLT Period) | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 87 (48.28%) | 37 / 89 (41.57%) | |
| Investigations | | | |
| Coronavirus Test Positive | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Weight Increased | | | |
| subjects affected / exposed | 9 / 87 (10.34%) | 12 / 89 (13.48%) | |
| occurrences (all) | 10 | 13 | |
| Injury, poisoning and procedural complications | | | |
| Clavicle Fracture | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Akathisia | | | |
| subjects affected / exposed | 4 / 87 (4.60%) | 4 / 89 (4.49%) | |
| occurrences (all) | 5 | 4 | |
| Headache | | | |
| subjects affected / exposed | 11 / 87 (12.64%) | 9 / 89 (10.11%) | |
| occurrences (all) | 12 | 12 | |
| Sedation | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 2 / 89 (2.25%) | |
| occurrences (all) | 0 | 2 | |
| Somnolence | | | |
| subjects affected / exposed | 9 / 87 (10.34%) | 7 / 89 (7.87%) | |
| occurrences (all) | 10 | 8 | |
| Tension Headache | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) Dysarthria subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 0 / 87 (0.00%) 0 | 0 / 89 (0.00%) 0 0 / 89 (0.00%) 0 | |
| Blood and lymphatic system disorders Erythropenia subjects affected / exposed occurrences (all) | 0 / 87 (0.00%) 0 | 0 / 89 (0.00%) 0 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Hyperthermia subjects affected / exposed occurrences (all) | 3 / 87 (3.45%) 3 0 / 87 (0.00%) 0 | 1 / 89 (1.12%) 1 0 / 89 (0.00%) 0 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 1 / 87 (1.15%) 1 | 2 / 89 (2.25%) 2 | |
| Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) | 1 / 87 (1.15%) 1 1 / 87 (1.15%) 1 | 0 / 89 (0.00%) 0 0 / 89 (0.00%) 0 | |
| Psychiatric disorders Major Depression subjects affected / exposed occurrences (all) Intentional Self-Injury subjects affected / exposed occurrences (all) Insomnia | 0 / 87 (0.00%) 0 1 / 87 (1.15%) 2 | 0 / 89 (0.00%) 0 0 / 89 (0.00%) 0 | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 8 / 87 (9.20%) | 4 / 89 (4.49%) | |
| occurrences (all) | 13 | 4 | |
| Anxiety | | | |
| subjects affected / exposed | 4 / 87 (4.60%) | 4 / 89 (4.49%) | |
| occurrences (all) | 7 | 5 | |
| Agitation | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 89 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Initial Insomnia | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Emotional Disorders | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Irritability | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Endocrine disorders | | | |
| Hyperprolactinaemia | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 89 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle Rigidity | | | |
| subjects affected / exposed | 4 / 87 (4.60%) | 0 / 89 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 5 / 89 (5.62%) | |
| occurrences (all) | 0 | 5 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 87 (4.60%) | 6 / 89 (6.74%) | |
| occurrences (all) | 7 | 7 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 2 / 89 (2.25%) | |
| occurrences (all) | 5 | 2 | |
| Coronavirus Pneumonia | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 89 (0.00%) | |
| occurrences (all) | 0 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 01 December 2017 | Clarified that the adequately trained clinician who confirms the diagnosis can also include an adult psychiatrist who is otherwise experienced in treating adolescents, informed consent/assent for rollover subjects must not be signed until the day of the Screening/Baseline visit for Trial 331-10-236, conversion period for de novo subjects lasts between 1-4 weeks duration, subjects should not be dosed from Trial 331-10-234 and Trial 331-10-236 on the same day for rollover subjects, added weekly (\pm 3 day) window parameters during open-label treatment, clarified the individual subject trial participation in the open-label treatment period will not exceed 24 months, monthly visits will be scheduled every 4 weeks, 2-month visits every 8 weeks and 3-month visits every 12 weeks, dose adjustments for brexpiprazole in the open-label treatment period for rollover subjects and de novo subjects after conversion, dose increases will be made weekly in 1 mg increments to a maximum of 4 mg/day, emphasized that the trial will be conducted on an outpatient basis, clarified the exclusion criteria 1, 2, 3, questions 4 or 5, deleted requirement in exclusion to have 3 time points collected for subjects with QTcF or QTcN corrections, assessment for the affected to be based on the last available measurement. Additionally, body weight and waist circumference, body temperature, were to be collected at every in-clinic visit, serum pregnancy test collection at Week 4, Months 6, 12 and 18 were added along with urine pregnancy test at Screening/Baseline for rollover subjects. Deleted process that OMRI will provide a copy of the CGAS for source. Clarified stimulant use for de novo subjects and maximum allowable dose levels of oral benzodiazepine rescue therapy, version of MedDRA to be used, updated packaging and labeling Section 8.1, changed assessment duration in C-SSRS, added reference number 12, updated section 15. |
| 13 September 2018 | Provided clarifications to support improved program facilitation and communication. Added history of electroconvulsive therapy to exclusions. Added birth control patch as an acceptable form of birth control. Removed inclusion criteria for subjects showing previous response to an antipsychotic. Added exclusion criteria for subjects known to have medication compliance issues that lead to intramuscular depot medication use. Added exclusion for subjects who report a true allergic response to aripiprazole or brexpiprazole, added exclusion of known poor metabolizers CYP2D6 or CYP3A4. Modified exclusion criteria for subjects considered treatment resistant to antipsychotic medication. Added in an exclusion for "subjects who participated in any clinical trial within the last 30 days prior to screening.". Added a possible extension of screening period following discussion with the medical monitor. Added recording of lifetime antipsychotic use to screening procedure. Added in a serum pregnancy test. Clarified that completion of trial will be registered by trial personnel in eSource. Removed filing of central laboratory reports with source documents. Added in total, low-density lipoprotein, and high-density lipoprotein for cholesterol clinical laboratory test. |
| 03 June 2019 | Clarification was added that subjects who were hospitalized for the entire duration of the 331-10-234 study will not be terminated if they are hospitalized in the 331-10-236 study for medical or psychosocial reasons. Added dispense investigational product to the Schedule of Assessments and clarified vital signs – refers to pulse and heart rate interchangeably throughout the protocol. Removed "predose" from the ECG assessment for Month 12. |
| 16 June 2020 | Introduced a COVID-19 Addendum for any protocol-specified activities that were not able to be performed or could not be performed due to COVID-19 considerations. Modifications were made regarding de novo subjects to support improved program facilitation. |

| | |
|----------------|---|
| 04 August 2021 | Changed the definition of a month duration from 4 weeks to 31 days (\pm 3 days) and removed the text referring to weeks for scheduling trial visits. Added the following text: Although there is a \pm 3-day visit window during the open-label treatment period, every attempt should be made to track each subject's monthly visits to ensure that the subject's final Month 24 visit meets the protocol's intended treatment duration of 2 calendar years. Changed the PQC reporting email address. |
|----------------|---|

Notes:

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 correct PIP number for 331-10-236 trial is EMA/PE/0000183866. Dummy PIP number is added in Paediatric regulatory details section as correct PIP number could not be accommodated due to database format constraint. |
|---|

Notes: