Clinical trial results:
A Multicenter, Double-Blind, Fixed-Dose, Long-Term Extension Trial of the Safety of Asenapine in Subjects Diagnosed with Bipolar 1 Disorder who Completed Protocol P05691 (formerly 041044) (Phase 3B, Protocol P05692 [formerly 041045])

Summary

EudraCT number	2010-018410-78
Trial protocol	BG
Global end of trial date	03 December 2014

Results information

Result version number	v1 (current)
This version publication date	31 January 2019
First version publication date	31 January 2019

Trial information

Trial identification

Sponsor protocol code	P05692

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01395992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Forest Research Institute, Inc., an affiliate of Allergan, plc
Sponsor organisation address	185 Hudson Street, Jersey City, United States, NJ 07302
Public contact	Willie Earley, Forest Research Institute, Inc., an affiliate of Allergan, plc, Willie.Earley@Allergan.com
Scientific contact	Willie Earley, Forest Research Institute, Inc., an affiliate of Allergan, plc, Willie.Earley@Allergan.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2014
Global end of trial reached?	Yes
Global end of trial date	03 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the long-term safety of asenapine in participants diagnosed with Bipolar 1 Disorder. Participants received a fixed dose of asenapine (either 5 or 10 milligram [mg] twice daily [BID]) for 26 weeks.

Protection of trial subjects:

This trial was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

This was a long-term extension trial for participants who had completed the 3-week short-term trial P05691. In the previous short-term trial, participants had been randomly assigned to receive a fixed dose of asenapine (either 5 mg or 10 mg BID) or placebo (BID) for 3 weeks.

Evidence for comparator: -

Actual start date of recruitment	09 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 125
Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Croatia: 2
Worldwide total number of subjects	165
EEA total number of subjects	22

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	162
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First participant enrolled: 9 May 2012; last participant completed: 3 Dec 2014. This trial was performed at 38 sites across the United States, Bulgaria, Ukraine, the Russian Federation, and Croatia.

Pre-assignment

Screening details:

A total of 165 participants who had previously completed the short-term randomized trial P05691 continued in the current extension trial (P05692). Participants randomly assigned to asenapine in P05691 were assigned the same treatment regimen in P05692; participants randomly assigned to placebo were assigned to asenapine 5 mg BID.

Period 1

Period 1 title	Enrollment through Start Treatment
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo / Asenapine 5 mg

Arm description:

In the previous short-term trial PO5691, participants were administered placebo BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast-dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 5 mg / Asenapine 5 mg

Arm description:

In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 5 mg Overall

Arm description:

In the previous short-term trial PO5691, participants were administered either placebo BID or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents

the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 10 mg / Asenapine 10 mg

Arm description:

In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

10 mg fast dissolving active asenapine tablets administered sublingually

Number of subjects in period 1	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 5 mg Overall
Started	61	53	114
Completed	60	53	113
Not completed	1	0	1
Did not meet protocol eligibility (not treated)	1	-	1

Number of subjects in period 1	Asenapine 10 mg / Asenapine 10 mg
Started	51
Completed	51
Not completed	0
Did not meet protocol eligibility (not treated)	-

Period 2

Period 2 title	Treatment through Trial Completion
Is this the baseline period?	Yes[1]
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo / Asenapine 5 mg

Arm description:

In the previous short-term trial PO5691, participants were administered placebo BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 5 mg / Asenapine 5 mg

Arm description:

In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 5 mg Overall

Arm description:

In the previous short-term trial PO5691, participants were administered either placebo BID or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.

Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

5 mg fast dissolving active asenapine tablets administered sublingually

Arm title	Asenapine 10 mg / Asenapine 10 mg

Arm description:

In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.

Arm type	Experimental

Investigational medicinal product name	Asenapine
Investigational medicinal product code	Asenapine
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

10 mg fast dissolving active asenapine tablets administered sublingually

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The participants who started Period 1 are those enrolled in this extension trial PO5692, 1 of whom did not receive study drug. The participants who started Period 2 are those who received study drug. The baseline demographics table presents data for participants treated, therefore Period 2 was set as the baseline period.

Number of subjects in period 2	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 5 mg Overall
Started	60	53	113
Completed	49	45	94
Not completed	11	8	19
Consent withdrawn by subject	2	2	4
Adverse event, non-fatal	1	1	2
Lost to follow-up	6	5	11
Protocol deviation	2	-	2

Number of subjects in period 2	Asenapine 10 mg / Asenapine 10 mg
Started	51
Completed	46
Not completed	5
Consent withdrawn by subject	4
Adverse event, non-fatal	-
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups[1]	
Reporting group title	Placebo / Asenapine 5 mg
Reporting group description:	
In the previous short-term trial PO5691, participants were administered placebo BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.	
Reporting group title	Asenapine 5 mg / Asenapine 5 mg
Reporting group description:	
In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.	
Reporting group title	Asenapine 5 mg Overall
Reporting group description:	
In the previous short-term trial PO5691, participants were administered either placebo BID or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.	
Reporting group title	Asenapine 10 mg / Asenapine 10 mg
Reporting group description:	
In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number enrolled in the trial presents participants who continued in this extension trial PO5692 from the previous short-term trial PO5691 ; 1 of these participants did not receive study drug. The participants who started Period 2 ("baseline period") are those who received study drug. The baseline demographics table presents data for participants treated, therefore Period 2 was set as the baseline period.

Reporting group values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 5 mg Overall
Number of subjects	60	53	113
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	43.9	44.8	44.4
standard deviation	± 10.9	± 9.55	± 10.25
Gender Categorical			
Units: Subjects			
Male	28	25	53
Female	32	28	60

Reporting group values	Asenapine 10 mg / Asenapine 10 mg	Total	
Number of subjects	51	277	
Age categorical			
Units: Subjects			

Age Continuous Units: years			
arithmetic mean	44.6		
standard deviation	± 10.66	-	
Gender Categorical Units: Subjects			
Male	22	128	
Female	29	149	

End points

End points reporting groups

Reporting group title	Placebo / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered placebo BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.

Reporting group title	Asenapine 5 mg / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.

Reporting group title	Asenapine 5 mg Overall

Reporting group description:

In the previous short-term trial PO5691, participants were administered either placebo BID or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.

Reporting group title	Asenapine 10 mg / Asenapine 10 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.

Reporting group title	Placebo / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered placebo BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.

Reporting group title	Asenapine 5 mg / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.

Reporting group title	Asenapine 5 mg Overall

Reporting group description:

In the previous short-term trial PO5691, participants were administered either placebo BID or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.

Reporting group title	Asenapine 10 mg / Asenapine 10 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

TEAEs were adverse events (AEs) which were first reported or worsened in severity on or after the first dose of study drug in the current extension trial (P05692) through: last dose date plus 7 days (for non-serious AEs) or last dose date plus 30 days (for Serious adverse events [SAEs]). The reported measure is the number of participants with ≥1 TEAE (and sub-categorised into treatment related TEAEs and severe TEAEs). Population for this analysis was the All Treated Set (ATS), defined as all randomized

participants from the short-term trial (PO5691) who received ≥1 dose study drug in the current extension trial (P05692).

End point type	Primary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to approximately 30 weeks)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for the end point "Number of Participants With Treatment-Emergent Adverse Events (TEAEs)".

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 5 mg Overall	Asenapine 10 mg / Asenapine 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	53	113	51
Units: Participants				
TEAE	41	29	70	26
Treatment related TEAE	28	15	43	15
Severe TEAE	3	2	5	3

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Trial P05691 Baseline in Young-Mania Rating Scale (Y-MRS) Total Score at Days 7, 28, 84, 182, and Study Endpoint

End point title	Change from Trial P05691 Baseline in Young-Mania Rating Scale (Y-MRS) Total Score at Days 7, 28, 84, 182, and Study Endpoint

End point description:

Y-MRS consists of responses to the following 11 items: elevated mood, increased motor activity energy, sexual interest, sleep, language-thought disorder, appearance, insight, irritability, speech - rate and amount, content and disruptive-agressive behavior. The scores from the 11 items are summed to give a Total Score ranging from 0 to 60, with a higher score indicating greater severity of symptoms. The reported measure is the change from short-term trial baseline (P05691) at each specified visit, analysed using an analysis of covariance (ANCOVA) model including fixed effects for treatment and investigative site (or pooled site) and baseline value as a covariate; improvement in symptoms is represented by negative values. Population for this analysis was the Full Analysis Set (FAS), defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Baseline (P05691) and Days 7, 28, 84, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
least squares mean (standard error)				
Day 7 (n=56, 48, 50)	-17.7 (± 1.13)	-18.9 (± 1.22)	-20.3 (± 1.2)	
Day 28 (n=47, 36, 38)	-19.4 (± 0.95)	-21.8 (± 1.12)	-23.4 (± 1.07)	
Day 84 (n=38, 33, 33)	-21.5 (± 0.87)	-22.4 (± 0.98)	-23.5 (± 0.96)	
Day 182 (n=32, 27, 23)	-22.7 (± 0.93)	-24.7 (± 1.06)	-23.5 (± 1.06)	
Study Endpoint (n=57, 50, 50)	-22.3 (± 0.94)	-22.9 (± 1.01)	-22 (± 1.01)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who are Y-MRS Responders at Days 7, 28, 84, 182, and Study Endpoint

End point title	Percentage of Participants who are Y-MRS Responders at Days 7, 28, 84, 182, and Study Endpoint

End point description:

A Y-MRS responder was defined as a participant who had a reduction from baseline of at least 50% in the Y-MRS Total Score at a post-baseline assessment. Responder status was assessed relative to the short-term trial baseline (P05691). Y-MRS consists of responses to the following 11 items: elevated mood, increased motor activity energy, sexual interest, sleep, language-thought disorder, appearance, insight, irritability, speech - rate and amount, content and disruptive-aggressive behaviour. The scores from the 11 items are summed to give a Total Score ranging from 0 to 60, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 28, 84, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: Percentage of responders				
number (not applicable)				
Day 7 (n=56, 48, 50)	66.1	68.8	80	
Day 28 (n=47, 36, 38)	72.3	86.1	92.1	
Day 84 (n=38, 33, 33)	92.1	84.8	93.9	
Day 182 (n=32, 27, 23)	90.6	96.3	91.3	
Study Endpoint (n=57, 50, 50)	87.7	88	84	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who are Y-MRS Remitters at Days 7, 28, 84, 182, and Study Endpoint

End point title	Percentage of Participants who are Y-MRS Remitters at Days 7, 28, 84, 182, and Study Endpoint

End point description:

A Y-MRS remitter was defined as a participant who had a Total Score of 12 or lower at a post-baseline assessment. Y-MRS consists of responses to the following 11 items: elevated mood, increased motor activity energy, sexual interest, sleep, language-thought disorder, appearance, insight, irritability, speech - rate and amount, content and disruptive-agressive behavior. The scores from the 11 items are summed to give a Total Score ranging from 0 to 60, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 28, 84, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: Percentage of participants				
number (not applicable)				
Day 7 (n=56, 48, 50)	55.4	62.5	62	
Day 28 (n=47, 36, 38)	59.6	83.3	86.8	
Day 84 (n=38, 33, 33)	73.7	81.8	72.7	
Day 182 (n=32, 27, 23)	81.3	96.3	78.3	
Study Endpoint (n=57, 50, 50)	77.2	86	68	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Trial P05691 Baseline in Clinical Global Impression – Bipolar Mania – Severity of Illness (CGI-BP-S) Overall Score at Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point title	Change from Trial P05691 Baseline in Clinical Global Impression – Bipolar Mania – Severity of Illness (CGI-BP-S)

	Overall Score at Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point description:

The CGI-BP-S is a score that measures the severity of overall bipolar illness. The score ranges on a scale from 1 to 7, where 1 is normal, and 7 is very severely ill. The reported measure is the change from short-term trial baseline (P05691) at each specified visit, analysed using an ANCOVA model including fixed effects for treatment and investigative site (or pooled site) and baseline value as a covariate; improvement in symptoms is represented by negative values. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Baseline and Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
least squares mean (standard error)				
Day 7 (n=56, 48, 50)	-1.9 (± 0.15)	-2 (± 0.16)	-2.1 (± 0.16)	
Day 14 (n=53, 44, 43)	-1.9 (± 0.14)	-2.2 (± 0.16)	-2.3 (± 0.16)	
Day 28 (n=47, 36, 37)	-2.1 (± 0.14)	-2.3 (± 0.17)	-2.2 (± 0.16)	
Day 56 (n=42, 36, 35)	-2.3 (± 0.13)	-2.6 (± 0.15)	-2.2 (± 0.15)	
Day 84 (n=38, 33, 33)	-2.2 (± 0.15)	-2.5 (± 0.17)	-2.3 (± 0.17)	
Day 112 (n=36, 25, 28)	-2.3 (± 0.16)	-2.5 (± 0.19)	-2.6 (± 0.18)	
Day 182 (n=32, 27, 23)	-2.6 (± 0.18)	-2.7 (± 0.2)	-2.8 (± 0.21)	
Study Endpoint (n=57, 50, 50)	-2.3 (± 0.16)	-2.4 (± 0.16)	-2.3 (± 0.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who are Clinical Global Impression – Bipolar Mania – Improvement (CGI-BP-I) Responders of Overall Bipolar Illness Score at Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point title	Percentage of Participants who are Clinical Global Impression – Bipolar Mania – Improvement (CGI-BP-I) Responders of Overall Bipolar Illness Score at Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point description:

A CGI-BP-I (Overall Bipolar Illness) responder was defined as a participant who had a score of 3 (minimally improved) or lower at a post-baseline assessment. Responder status was assessed relative to the short-term trial baseline (P05691). The CGI-BP-I (Overall Bipolar Illness) is a score on a 7-point scale for assessing the change from preceding phase of overall symptoms of bipolar disorder during the treatment of an acute episode or in longer term illness prophylaxis. Compared to the baseline, the CGI-BP-I overall score ranges from 1 = very much improved since initiating treatment, to 7 = very much worse since initiating treatment. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 14, 28, 56, 84, 112, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: Percentage of participants				
number (not applicable)				
Day 7 (n=56, 48, 50)	89.3	89.6	88	
Day 14 (n=53, 44, 43)	86.8	81.8	88.4	
Day 28 (n=47, 36, 37)	89.4	88.9	83.8	
Day 56 (n=42, 36, 35)	95.2	94.4	85.7	
Day 84 (n=38, 33, 33)	94.7	90.9	87.9	
Day 112 (n=36, 25, 28)	91.7	92	92.9	
Day 182 (n=32, 27, 23)	90.6	92.6	87	
Study Endpoint (n=57, 50, 50)	89.5	84	80	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Trial P05691 Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Days 7, 182, and Study Endpoint

End point title	Change from Trial P05691 Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Days 7, 182, and Study Endpoint

End point description:

The MADRS measures depression and consists of 10 items, each rated on a scale from 0 to 6. The MADRS Total Score sums the scores from the 10 items, ranging from 0 to 60, with a higher numeric rating implying a greater degree of symptom severity. The reported measure is the change from short-term trial baseline (P05691) at each specified visit, analysed using an ANCOVA model including fixed effects for treatment and investigative site (or pooled site) and baseline value as a covariate; improvement in symptoms is represented by negative values. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Baseline and Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
least squares mean (standard error)				
Day 7 (n=56, 48, 50)	-7 (± 0.84)	-6 (± 0.9)	-6.6 (± 0.9)	
Day 182 (n=32, 27, 23)	-7.5 (± 1.28)	-7.7 (± 1.43)	-7.8 (± 1.46)	
Study Endpoint (n=57, 50, 50)	-6.9 (± 1.11)	-5.6 (± 1.17)	-5.9 (± 1.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Positive And Negative Syndrome Scale (PANSS) Total Score at Days 7, 182, and Study Endpoint

End point title	Positive And Negative Syndrome Scale (PANSS) Total Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Total Score measures symptoms of schizophrenia and consists of responses to 30 items: 7 items from the positive subscale (P1-P7), 7 items from the negative subscale (N1-N7) and 16 items from the general psychopathology subscale (G1-G16). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Total Score sums the scores from all 30 items, and ranges from 30 to 210, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	49.1 (± 10.82)	48.2 (± 11.39)	46 (± 11.07)	
Day 182 (n=32, 27, 23)	45.6 (± 10.39)	44.6 (± 12.41)	42.4 (± 10.21)	
Study Endpoint (n=57, 50, 50)	48.3 (± 10.93)	47 (± 11.95)	47.5 (± 12.97)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Negative Subscale Score at Days 7, 182, and Study Endpoint

End point title	PANSS Negative Subscale Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Negative subscale measures symptoms of schizophrenia and consists of responses to 7 items (N1-N7). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Negative subscale sums the scores from all 7 items and ranges from 7 to 49, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	11.4 (± 4.1)	11.7 (± 3.62)	10.7 (± 3.19)	
Day 182 (n=32, 27, 23)	11.6 (± 4.21)	11.7 (± 3.87)	10.3 (± 2.85)	
Study Endpoint (n=57, 50, 50)	11.9 (± 4.55)	11.8 (± 3.56)	11.2 (± 3.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Positive Subscale Score at Days 7, 182, and Study Endpoint

End point title	PANSS Positive Subscale Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Positive subscale measures symptoms of schizophrenia and consists of responses to 7 items (P1-P7). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Positive subscale sums the scores from all 7 items and ranges from 7 to 49, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	12.1 (± 3.3)	11.3 (± 3.32)	11.3 (± 3.69)	
Day 182 (n=32, 27, 23)	10.2 (± 2.94)	10 (± 3.45)	10 (± 2.72)	
Study Endpoint (n=57, 50, 50)	11.1 (± 3.1)	10.6 (± 3.45)	11 (± 3.59)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS General Psychopathology Subscale Score at Days 7, 182, and Study Endpoint

End point title	PANSS General Psychopathology Subscale Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS General Psychopathology subscale measures symptoms of schizophrenia and consists of responses to 16 items (G1-G16). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS General Psychopathology subscale sums the scores from all 16 items and ranges from 16 to 112, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	25.6 (± 5.54)	25.2 (± 6.07)	24 (± 5.98)	
Day 182 (n=32, 27, 23)	23.8 (± 5.54)	22.9 (± 7.26)	22 (± 5.81)	
Study Endpoint (n=57, 50, 50)	25.3 (± 5.69)	24.6 (± 7.13)	25.3 (± 7.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Marder Factor Positive Symptom Score at Days 7, 182, and Study Endpoint

End point title	PANSS Marder Factor Positive Symptom Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Marder Factor Positive symptom score measures symptoms of schizophrenia and consists of responses to 8 items (P1,P3,P5,P6,N7,G1,G9,G12). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Marder Factor Positive symptom score sums the scores from all 8 items and ranges from 8 to 56, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	13.5 (± 3.88)	12.7 (± 3.74)	11.8 (± 3.25)	
Day 182 (n=32, 27, 23)	11.4 (± 3.22)	11.4 (± 4.38)	10.7 (± 2.36)	
Study Endpoint (n=57, 50, 50)	12.3 (± 3.61)	11.9 (± 4.18)	11.7 (± 3.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Marder Factor Negative Symptom Score at Days 7, 182, and Study Endpoint

End point title	PANSS Marder Factor Negative Symptom Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Marder Factor Negative symptom score measures symptoms of schizophrenia and consists of responses to 7 items (N1,N2,N3,N4,N6,G7,G16). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Marder Factor Negative symptom score sums the scores from all 7 items and ranges from 7 to 49, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	10.6 (± 4.15)	10.5 (± 3.36)	9.8 (± 3)	
Day 182 (n=32, 27, 23)	11.1 (± 4.29)	10.9 (± 3.3)	10 (± 2.87)	
Study Endpoint (n=57, 50, 50)	11.4 (± 4.83)	10.9 (± 3.67)	10.7 (± 3.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Marder Factor Disorganized Thought Symptom Score at Days 7, 182, and Study Endpoint

End point title	PANSS Marder Factor Disorganized Thought Symptom Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Marder Factor Disorganized Thought symptom score measures symptoms of schizophrenia and consists of responses to 7 items (P2,N5,G5,G10,G11,G13,G15). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Marder Factor Disorganized Thought symptom score sums the scores from all 7 items and ranges from 7 to 49, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	11.3 (± 3.01)	11.4 (± 2.9)	11.4 (± 3.13)	
Day 182 (n=32, 27, 23)	10.3 (± 2.89)	10.8 (± 3.59)	10.3 (± 3.33)	
Study Endpoint (n=57, 50, 50)	10.9 (± 2.91)	11 (± 3.37)	11.1 (± 3.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Marder Factor Hostility/Excitement Symptom Score at Days 7, 182, and Study Endpoint

End point title	PANSS Marder Factor Hostility/Excitement Symptom Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Marder Factor Hostility/Excitement symptom score measures symptoms of schizophrenia and consists of responses to 4 items (P4,P7,G8,G14). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Marder Factor Hostility/Excitement symptom score sums the score from all 4 items and ranges from 4 to 28, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	7 (± 2.41)	6.7 (± 2.51)	7 (± 2.98)	
Day 182 (n=32, 27, 23)	5.9 (± 1.83)	5.5 (± 1.89)	5.4 (± 1.83)	
Study Endpoint (n=57, 50, 50)	6.6 (± 2.27)	6 (± 2.29)	6.9 (± 3.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: PANSS Marder Factor Anxiety/Depression Symptom Score at Days 7, 182, and Study Endpoint

End point title	PANSS Marder Factor Anxiety/Depression Symptom Score at Days 7, 182, and Study Endpoint

End point description:

The PANSS Marder Factor Anxiety/Depression symptom score measures symptoms of schizophrenia and consists of responses to 4 items (G2,G3,G4,G6). Responses to each item range from 1 = absence of symptom, to 7 = most extreme symptoms. The PANSS Marder Factor Anxiety/Depression symptom score sums the scores from all 4 items and ranges from 4 to 28, with a higher score indicating greater severity of symptoms. Population for this analysis was the FAS, defined as all randomized participants from PO5691 who received ≥1 dose of study drug in PO5692 and had ≥1 post-baseline Y-MRS Total Score assessment.

End point type	Secondary

End point timeframe:

Days 7, 182, and Study Endpoint

End point values	Placebo / Asenapine 5 mg	Asenapine 5 mg / Asenapine 5 mg	Asenapine 10 mg / Asenapine 10 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	52	50	
Units: units on a scale				
arithmetic mean (standard deviation)				
Day 7 (n=56, 48, 50)	6.7 (± 2.57)	7 (± 3.13)	6 (± 2.99)	
Day 182 (n=32, 27, 23)	6.8 (± 2.69)	6 (± 2.92)	6 (± 2.66)	
Study Endpoint (n=57, 50, 50)	7.1 (± 2.75)	7.2 (± 3.55)	7.1 (± 3.64)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 30 days after last dose of study drug (up to approximately 30 weeks).

Adverse event reporting additional description:

Analysis population was the ATS which included all randomized participants from the short-term trial (PO5691) who received ≥1 dose of study drug in the current extension trial (PO5692).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered placebo for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks.

Reporting group title	Asenapine 5 mg Overall

Reporting group description:

In the previous short-term trial PO5691, participants were administered either placebo or one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were administered one 5 mg asenapine tablet BID for 26 weeks. The 'asenapine 5 mg overall' arm represents the 'placebo / asenapine 5 mg' and 'asenapine 5 mg / asenapine 5 mg' arms combined.

Reporting group title	Asenapine 10 mg / Asenapine 10 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 10 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 10 mg asenapine tablet BID) for 26 weeks.

Reporting group title	Asenapine 5 mg / Asenapine 5 mg

Reporting group description:

In the previous short-term trial PO5691, participants were administered one 5 mg asenapine tablet BID for 21 days; in the current extension trial (PO5692), participants were assigned to the same treatment regimen (ie, one 5 mg asenapine tablet BID) for 26 weeks.

Serious adverse events	Placebo / Asenapine 5 mg	Asenapine 5 mg Overall	Asenapine 10 mg / Asenapine 10 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)	3 / 113 (2.65%)	2 / 51 (3.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 60 (0.00%)	0 / 113 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 113 (0.88%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar I Disorder			
subjects affected / exposed	1 / 60 (1.67%)	1 / 113 (0.88%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major Depression			
subjects affected / exposed	1 / 60 (1.67%)	1 / 113 (0.88%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 60 (0.00%)	0 / 113 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Asenapine 5 mg / Asenapine 5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar I Disorder			

subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Major Depression			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mania			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo / Asenapine 5 mg	Asenapine 5 mg Overall	Asenapine 10 mg / Asenapine 10 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 60 (56.67%)	59 / 113 (52.21%)	33 / 51 (64.71%)
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	4 / 60 (6.67%)	6 / 113 (5.31%)	2 / 51 (3.92%)
occurrences (all)	8	10	3
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 60 (1.67%)	4 / 113 (3.54%)	1 / 51 (1.96%)
occurrences (all)	1	4	1
Nervous system disorders			
Akathisia			
subjects affected / exposed	5 / 60 (8.33%)	7 / 113 (6.19%)	10 / 51 (19.61%)
occurrences (all)	7	9	10
Dysgeusia			
subjects affected / exposed	1 / 60 (1.67%)	3 / 113 (2.65%)	3 / 51 (5.88%)
occurrences (all)	1	3	3
Headache			
subjects affected / exposed	5 / 60 (8.33%)	7 / 113 (6.19%)	5 / 51 (9.80%)
occurrences (all)	8	11	5

Sedation			
subjects affected / exposed	6 / 60 (10.00%)	10 / 113 (8.85%)	6 / 51 (11.76%)
occurrences (all)	6	10	6
Somnolence			
subjects affected / exposed	7 / 60 (11.67%)	12 / 113 (10.62%)	6 / 51 (11.76%)
occurrences (all)	7	12	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 113 (0.88%)	3 / 51 (5.88%)
occurrences (all)	0	1	4
Dry Mouth			
subjects affected / exposed	7 / 60 (11.67%)	10 / 113 (8.85%)	2 / 51 (3.92%)
occurrences (all)	7	10	2
Hypoaesthesia Oral			
subjects affected / exposed	6 / 60 (10.00%)	9 / 113 (7.96%)	10 / 51 (19.61%)
occurrences (all)	6	9	11
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	4 / 113 (3.54%)	0 / 51 (0.00%)
occurrences (all)	1	5	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 60 (0.00%)	4 / 113 (3.54%)	3 / 51 (5.88%)
occurrences (all)	0	5	5
Insomnia			
subjects affected / exposed	6 / 60 (10.00%)	9 / 113 (7.96%)	4 / 51 (7.84%)
occurrences (all)	6	9	4
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	7 / 60 (11.67%)	10 / 113 (8.85%)	2 / 51 (3.92%)
occurrences (all)	7	10	2
Metabolism and nutrition disorders			
Increased Appetite			
subjects affected / exposed	5 / 60 (8.33%)	6 / 113 (5.31%)	2 / 51 (3.92%)
occurrences (all)	5	6	2

Non-serious adverse events	Asenapine 5 mg / Asenapine 5 mg		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	25 / 53 (47.17%)		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Nervous system disorders			
Akathisia			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Dysgeusia			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	3		
Sedation			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Somnolence			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Dry Mouth			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Hypoaesthesia Oral			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Toothache			

subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 4 / 53 (7.55%) 5 3 / 53 (5.66%) 3		
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	 3 / 53 (5.66%) 3		
Metabolism and nutrition disorders Increased Appetite subjects affected / exposed occurrences (all)	 1 / 53 (1.89%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2011	• Text regarding drug-induced liver injury (as a closely monitored event [CME]) was revised based on latest guidance of the Food and Drug Administration (FDA). • A new CME of 'suicidal ideation and/or behaviour' was added. • The SAE section was updated to include 'cancer' as SAE outcome #6. • The urinalysis tests listed as procedures for safety assessments was revised. • "Incidents associated with the device" was deleted from the list of events requiring expedited reporting of safety observations by the investigator to the sponsor since this was not relevant to the trial. • Sections in the protocol relating to medication error, potential medication error, and incident were deleted.
10 October 2011	• A new CME of 'drug hypersensitivity reactions' was added. • Text relating to the monitoring of liver enzymes was updated to be consistent with FDA Drug Induced Liver Injury guidance. • "Antiemetics containing dopamine agonists" was corrected to "Antiemetics containing dopamine antagonists" in Table 2 of the protocol which described medications, supplements and other substances and treatments prohibited during treatment with trial medication.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported