



## Clinical trial results:

### **A Multicenter, Randomized, Double-Blind, Fixed-Dose, 6-Week Trial of the Efficacy and Safety of Asenapine Compared With Placebo Using Olanzapine as an Active Control in Subjects With an Acute Exacerbation of Schizophrenia (Phase 3B, Protocol P05688 [formerly 041038]).**

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

EudraCT number	2010-018407-28
Trial protocol	BG
Global end of trial date	09 September 2014

## Results information

Result version number	v1 (current)
This version publication date	26 February 2016
First version publication date	26 February 2016

## Trial information

### Trial identification

Sponsor protocol code	P05688
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01617187
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol number: MK-8274-001

Notes:

## Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	09 September 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 September 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this trial is to assess effect of asenapine 2.5 and 5 mg sublingually twice daily (BID) compared with placebo in treatment of schizophrenia (overall symptoms) as measured by the Positive and Negative Syndrome Scale (PANSS). Olanzapine administered 15 mg orally once daily (QD) was used as an active control. Primary hypothesis is that at least one of the asenapine doses is superior to placebo in improving schizophrenia symptoms as measured by change from Baseline in PANSS total score at Day 42. The first key secondary hypothesis is that at least one of the asenapine doses is superior to placebo in improving schizophrenia symptoms as measured by change from Baseline in Clinical Global Impression Scale-Severity (CGI-S) score at Day 42. The second key secondary hypothesis is that at least one of the asenapine doses is superior to placebo in improving schizophrenia symptoms as measured by rate of PANSS responders ( $\geq 30\%$  Reduction From Baseline in PANSS Total Score) at Day 42.

Protection of trial subjects:

This study 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: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	8 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 53
Country: Number of subjects enrolled	Romania: 37
Country: Number of subjects enrolled	Russian Federation: 73
Country: Number of subjects enrolled	Ukraine: 38
Country: Number of subjects enrolled	United States: 140
Country: Number of subjects enrolled	Croatia: 19
Worldwide total number of subjects	360
EEA total number of subjects	109

Notes:

<b>Subjects enrolled per age group</b>	
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)	357
From 65 to 84 years	3
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

One participant randomized to asenapine 2.5 mg BID did not receive study drug but was recorded in clinical database as completing the study. In Subject Disposition table, this participant is presented as Not Completed in period "Randomization through Start Treatment" (Not Treated).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Asenapine 2.5 mg BID

Arm description:

Participants were administered one 2.5 mg asenapine tablet BID for 42 days

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

Dosage and administration details:

2.5 mg or 5 mg fast dissolving active asenapine tablets administered sublingually

Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally

<b>Arm title</b>	Asenapine 5 mg BID
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Arm description:

Participants were administered one 5 mg asenapine tablet BID for 42 days

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

Dosage and administration details:

2.5 mg or 5 mg fast dissolving active asenapine tablets administered sublingually

Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally	
<b>Arm title</b>	Olanzapine 15 mg QD
Arm description:	
Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered	
Arm type	Active comparator
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 and 10 mg film-coated active olanzapine tablets administered orally QD. The time of the active olanzapine dose (either morning or evening) is not disclosed in order to preserve blinding	
Investigational medicinal product name	Placebo Asenapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use
Dosage and administration details:	
Fast dissolving placebo asenapine tablets (to match 2.5 mg and 5 mg active asenapine tablets) administered sublingually	
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally	
<b>Arm title</b>	Placebo BID
Arm description:	
Participants were administered placebo tablets BID for 42 days	
Arm type	Placebo
Investigational medicinal product name	Placebo Asenapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use
Dosage and administration details:	
Fast dissolving placebo asenapine tablets (to match 2.5 mg and 5 mg active asenapine tablets) administered sublingually	
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
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Dosage and administration details:

Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally

<b>Number of subjects in period 1</b>	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD
Started	98	113	46
Completed	97	113	46
Not completed	1	0	0
Not Treated: Completed study in database	1	-	-
Not Treated: Administrative Reason	-	-	-
Not Treated: Adverse Event	-	-	-

<b>Number of subjects in period 1</b>	Placebo BID
Started	103
Completed	101
Not completed	2
Not Treated: Completed study in database	-
Not Treated: Administrative Reason	1
Not Treated: Adverse Event	1

<b>Period 2</b>	
Period 2 title	Treatment through Study Completion
Is this the baseline period?	Yes <sup>[1]</sup>
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject
<b>Arms</b>	
Are arms mutually exclusive?	Yes
<b>Arm title</b>	Asenapine 2.5 mg BID
Arm description:	
Participants were administered one 2.5 mg asenapine tablet BID for 42 days	
Arm type	Experimental

Investigational medicinal product name	Asenapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use
Dosage and administration details:	
2.5 mg or 5 mg fast dissolving active asenapine tablets administered sublingually	
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally	
<b>Arm title</b>	Asenapine 5 mg BID
Arm description:	
Participants were administered one 5 mg asenapine tablet BID for 42 days	
Arm type	Experimental
Investigational medicinal product name	Asenapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use
Dosage and administration details:	
2.5 mg or 5 mg fast dissolving active asenapine tablets administered sublingually	
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally	
<b>Arm title</b>	Olanzapine 15 mg QD
Arm description:	
Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered	
Arm type	Active comparator
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 and 10 mg film-coated active olanzapine tablets administered orally QD. The time of the active olanzapine dose (either morning or evening) is not disclosed in order to preserve blinding	
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:  
Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally

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

Dosage and administration details:

Fast dissolving placebo asenapine tablets (to match 2.5 mg and 5 mg active asenapine tablets) administered sublingually

<b>Arm title</b>	Placebo BID
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Arm description:

Participants were administered placebo tablets BID for 42 days

Arm type	Placebo
Investigational medicinal product name	Placebo Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated placebo olanzapine tablets (to match 5 and 10 mg active olanzapine tablets) administered orally

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

Dosage and administration details:

Fast dissolving placebo asenapine tablets (to match 2.5 mg and 5 mg 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 randomized, 3 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.

<b>Number of subjects in period 2<sup>[2]</sup></b>	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD
Started	97	113	46
Completed	86	102	41
Not completed	11	11	5
Consent withdrawn by subject	5	8	3
Adverse event, non-fatal	1	1	-
Lost to follow-up	4	2	2
Protocol deviation	1	-	-

<b>Number of subjects in period 2<sup>[2]</sup></b>	Placebo BID
Started	101



Completed	91
Not completed	10
Consent withdrawn by subject	6
Adverse event, non-fatal	1
Lost to follow-up	2
Protocol deviation	1

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Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number enrolled in the trial presents participants randomized; 3 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.

## Baseline characteristics

### Reporting groups

Reporting group title	Asenapine 2.5 mg BID
Reporting group description:	
Participants were administered one 2.5 mg asenapine tablet BID for 42 days	
Reporting group title	Asenapine 5 mg BID
Reporting group description:	
Participants were administered one 5 mg asenapine tablet BID for 42 days	
Reporting group title	Olanzapine 15 mg QD
Reporting group description:	
Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered	
Reporting group title	Placebo BID
Reporting group description:	
Participants were administered placebo tablets BID for 42 days	

Reporting group values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD
Number of subjects	97	113	46
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	41.5	39.1	40.8
standard deviation	± 10.79	± 10.68	± 11.15
Gender categorical			
Units: Subjects			
Female	39	44	18
Male	58	69	28
Positive and Negative Syndrome Scale (PANSS) total score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS total score (30 items) ranged from 30 to 210 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (Full Analysis Set [FAS]): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	93.3	95.8	92.7
standard deviation	± 11.1	± 13.77	± 10.47
Clinical Global Impression Scale-Severity (CGI-S) score			
CGI-S is a 7-point scale for assessing the global severity of the participant's illness, with ratings from 1=normal, not ill to 7=very severely ill. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	4.8	4.9	4.8
standard deviation	± 0.64	± 0.64	± 0.61
Body Weight			
Units: kg			

arithmetic mean	81.6	78.6	80.7
standard deviation	± 17.73	± 17.88	± 17.79
PANSS negative subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS negative subscale score (7 PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	23.5	24.1	23.4
standard deviation	± 4.47	± 4.5	± 3.96
PANSS positive subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS positive subscale score (7 PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	24.4	25.5	24.6
standard deviation	± 4.05	± 4.76	± 3.46
PANSS general psychopathology subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS general psychopathology subscale score (16 PANSS items) ranged from 16 to 112 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	45.5	46.3	44.7
standard deviation	± 6.05	± 6.87	± 6.2
PANSS Marder factor positive symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor positive symptom score (calculated from value of 8 identified PANSS items) ranged from 8 to 56 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	29.3	30	29
standard deviation	± 5.02	± 5.05	± 4.69
PANSS Marder factor negative symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor negative symptom score (calculated from value of 7 identified PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	22.6	23	23
standard deviation	± 4.3	± 4.66	± 4.44
PANSS Marder factor disorganized thought symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor disorganized thought symptom score (calculated from value of 7 identified PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for			

efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	21.5	22.6	21.2
standard deviation	± 4.32	± 4.93	± 4.29
PANSS Marder factor hostility/excitement symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor hostility/excitement symptom score (calculated from value of 4 identified PANSS items) ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	9	9.4	8.7
standard deviation	± 2.99	± 3.49	± 3.11
PANSS Marder factor anxiety/depression symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor anxiety/depression symptom score (calculated from value of 4 identified PANSS items) ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	11	10.9	10.9
standard deviation	± 2.97	± 3.13	± 3.62

Reporting group values	Placebo BID	Total	
Number of subjects	101	357	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	41.4		
standard deviation	± 12.05	-	
Gender categorical			
Units: Subjects			
Female	47	148	
Male	54	209	
Positive and Negative Syndrome Scale (PANSS) total score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS total score (30 items) ranged from 30 to 210 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (Full Analysis Set [FAS]): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	93.4		
standard deviation	± 11.16	-	
Clinical Global Impression Scale-Severity (CGI-S) score			
CGI-S is a 7-point scale for assessing the global severity of the participant's illness, with ratings from 1=normal, not ill to 7=very severely ill. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			

Units: score on a scale arithmetic mean standard deviation	4.8 ± 0.61	-	
Body Weight Units: kg arithmetic mean standard deviation	77.1 ± 17.56	-	
PANSS negative subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS negative subscale score (7 PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale arithmetic mean standard deviation	23.9 ± 4.22	-	
PANSS positive subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS positive subscale score (7 PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale arithmetic mean standard deviation	24.6 ± 3.88	-	
PANSS general psychopathology subscale score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS general psychopathology subscale score (16 PANSS items) ranged from 16 to 112 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale arithmetic mean standard deviation	44.9 ± 6.05	-	
PANSS Marder factor positive symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor positive symptom score (calculated from value of 8 identified PANSS items) ranged from 8 to 56 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale arithmetic mean standard deviation	29.4 ± 4.36	-	
PANSS Marder factor negative symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor negative symptom score (calculated from value of 7 identified PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale arithmetic mean standard deviation	22.8 ± 4.76	-	

PANSS Marder factor disorganized thought symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor disorganized thought symptom score (calculated from value of 7 identified PANSS items) ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	21.6		
standard deviation	± 4.42	-	
PANSS Marder factor hostility/excitement symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor hostility/excitement symptom score (calculated from value of 4 identified PANSS items) ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	8.8		
standard deviation	± 3.22	-	
PANSS Marder factor anxiety/depression symptom score			
The PANSS is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS Marder factor anxiety/depression symptom score (calculated from value of 4 identified PANSS items) ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Summary statistics presented are for efficacy population (FAS): N=96, 111, 45 and 99 for asenapine 2.5 mg BID, asenapine 5 mg BID, olanzapine 15 mg QD and placebo BID groups, respectively.			
Units: score on a scale			
arithmetic mean	10.7		
standard deviation	± 2.96	-	

## End points

### End points reporting groups

Reporting group title	Asenapine 2.5 mg BID
Reporting group description: Participants were administered one 2.5 mg asenapine tablet BID for 42 days	
Reporting group title	Asenapine 5 mg BID
Reporting group description: Participants were administered one 5 mg asenapine tablet BID for 42 days	
Reporting group title	Olanzapine 15 mg QD
Reporting group description: Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered	
Reporting group title	Placebo BID
Reporting group description: Participants were administered placebo tablets BID for 42 days	
Reporting group title	Asenapine 2.5 mg BID
Reporting group description: Participants were administered one 2.5 mg asenapine tablet BID for 42 days	
Reporting group title	Asenapine 5 mg BID
Reporting group description: Participants were administered one 5 mg asenapine tablet BID for 42 days	
Reporting group title	Olanzapine 15 mg QD
Reporting group description: Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered	
Reporting group title	Placebo BID
Reporting group description: Participants were administered placebo tablets BID for 42 days	

### Primary: Change From Baseline in PANSS Total Score at Day 42

End point title	Change From Baseline in PANSS Total Score at Day 42
End point description: The PANSS is a 30-item clinician-rated instrument for assessing schizophrenia symptoms. It consists of 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology subscale (16 items). For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS total score for each participant was sum of the rating assigned to each of the 30 PANSS items, and ranged from 30 to 210 with a higher score indicating greater severity of symptoms. The reported measure is the change from baseline at Day 42; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received $\geq 1$ dose of study drug and had both a baseline and $\geq 1$ post-baseline PANSS Total Score.	
End point type	Primary
End point timeframe: Baseline and Day 42	

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)	-17.4 ( $\pm$ 1.8)	-21.7 ( $\pm$ 1.6)	-21.6 ( $\pm$ 2.32)	-16.2 ( $\pm$ 1.71)

## Statistical analyses

Statistical analysis title	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, Mixed Model Repeated Measures (MMRM) model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6043 <sup>[1]</sup>
Method	MMRM
Parameter estimate	Least Squares (LS) means difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	3.6
Variability estimate	Standard error of the mean
Dispersion value	2.46

Notes:

[1] - Adjusted p-value from graphical approach to control Type 1 error rate among primary and secondary efficacy hypotheses

Statistical analysis title	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0356 <sup>[2]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-5.5



Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	2.32

Notes:

[2] - Adjusted p-value from graphical approach to control Type 1 error rate among primary and secondary efficacy hypotheses

<b>Statistical analysis title</b>	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0587 <sup>[3]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	2.86

Notes:

[3] - Unadjusted p-value

## Secondary: Change From Baseline in CGI-S Score at Day 42

End point title	Change From Baseline in CGI-S Score at Day 42
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End point description:

Change from baseline in CGI-S score at Day 42 is a Key Secondary Outcome Measure. CGI-S is a 7-point scale for assessing the global severity of the participant's illness, with ratings from 1=normal, not ill to 7=very severely ill. The reported measure is the change from baseline at Day 42; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received ≥1 dose of study drug and had both a baseline and ≥1 post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Day 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)	-0.9 ( $\pm$ 0.11)	-1.2 ( $\pm$ 0.1)	-1.1 ( $\pm$ 0.14)	-1 ( $\pm$ 0.11)

## Statistical analyses

Statistical analysis title	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" below is sum of participants in FAS population in the 2 treatment groups compared and is automatically calculated by data entry system; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants. Confirmative testing of asenapine versus placebo was performed only if both asenapine doses were statistically superior to placebo in reduction from baseline in PANSS Total Score at Day 42.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9083 <sup>[4]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[4] - Unadjusted p-value

Statistical analysis title	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" below is sum of participants in FAS population in the 2 treatment groups compared and is automatically calculated by data entry system; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants. Confirmative testing of asenapine versus placebo was performed only if both asenapine doses were statistically superior to placebo in reduction from baseline in PANSS Total Score at Day 42.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0601 <sup>[5]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[5] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3898 <sup>[6]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[6] - Unadjusted p-value

### **Secondary: Percentage of Participants Who Are PANSS Responders (≥30% Reduction From Baseline in PANSS Total Score) at Day 42**

End point title	Percentage of Participants Who Are PANSS Responders (≥30% Reduction From Baseline in PANSS Total Score) at Day 42
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End point description:

Rate of PANSS responders at Day 42 is a Key Secondary Outcome Measure. A PANSS responder was defined as a participant who had a reduction from baseline of at least 30% in the PANSS total score at a post-baseline assessment. The PANSS is a 30-item clinician-rated instrument for assessing schizophrenia symptoms. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The Total score is the sum of the ratings for the individual items, and ranged from 30 to 210 with a higher score indicating greater severity of symptoms. Missing data were imputed by Last Observation Carried Forward (LOCF). Population for this analysis was FAS, defined as randomized participants who received ≥1 dose of study drug and had both a baseline and ≥1 post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Day 42

<b>End point values</b>	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: percentage of participants				
number (not applicable)	14.6	25.2	26.7	19.2

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group
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Statistical analysis description:

Confirmative testing of asenapine versus placebo for this measure was to be performed only if both asenapine doses were statistically superior to placebo in reduction from baseline in PANSS Total Score at Day 42.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.37 <sup>[7]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[7] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group
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Statistical analysis description:

Confirmative testing of asenapine versus placebo for this measure was to be performed only if both asenapine doses were statistically superior to placebo in reduction from baseline in PANSS Total Score at Day 42.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1708 <sup>[8]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[8] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.262 <sup>[9]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[9] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

## Secondary: Change From Baseline in Body Weight at Day 42

End point title	Change From Baseline in Body Weight at Day 42
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End point description:

Change from baseline in body weight at Day 42 is the Key Safety Outcome Measure. Population for this analysis was all randomized participants who received  $\geq 1$  dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline and Day 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	113	46	101
Units: kg				
least squares mean (standard error)	1.3 ( $\pm$ 0.38)	1.3 ( $\pm$ 0.33)	2.4 ( $\pm$ 0.47)	0.3 ( $\pm$ 0.35)

## Statistical analyses

Statistical analysis title	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the all subjects treated population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire all subjects treated population in all 4 treatment groups, which includes 357 participants.

Comparison groups	Asenapine 2.5 mg BID v Olanzapine 15 mg QD
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Number of subjects included in analysis	143
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	= 0.0491 <sup>[10]</sup>
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Method	MMRM
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Parameter estimate	LS means difference
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Point estimate	-1.2
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-2.4
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upper limit	0
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Variability estimate	Standard error of the mean
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Dispersion value	0.6
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Notes:

[10] - p-value adjusted for multiple comparisons using Hochberg's method

Statistical analysis title	Comparison by Treatment Group
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the all subjects treated population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire all subjects treated population in all 4 treatment groups, which includes 357 participants.

Comparison groups	Asenapine 5 mg BID v Olanzapine 15 mg QD
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0491 <sup>[11]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.57

**Notes:**

[11] - p-value adjusted for multiple comparisons using Hochberg's method

<b>Statistical analysis title</b>	Comparison by Treatment Group
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the all subjects treated population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire all subjects treated population in all 4 treatment groups, which includes 357 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0567 <sup>[12]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.51

**Notes:**

[12] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the all subjects treated population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire all subjects treated population in all 4 treatment groups, which includes 357 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0391 <sup>[13]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.48

Notes:

[13] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the all subjects treated population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire all subjects treated population in all 4 treatment groups, which includes 357 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003 <sup>[14]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3.3
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[14] - Unadjusted p-value

## Secondary: Change From Baseline in PANSS Total Score at Days 4, 7, 14, 21, 28 and 35

End point title	Change From Baseline in PANSS Total Score at Days 4, 7, 14, 21, 28 and 35
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End point description:

The PANSS is a 30-item clinician-rated instrument for assessing schizophrenia symptoms. It consists of 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology subscale (16 items). For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS total score for each participant was sum of the rating assigned to each of the 30 PANSS items, and ranged from 30 to 210 with a higher score indicating greater severity of symptoms. The reported measure is the change from baseline; improvement in symptoms is represented by

negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
End point timeframe:	
Baseline and Days 4, 7, 14, 21, 28 and 35	

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-4 ( $\pm$ 0.8)	-4.9 ( $\pm$ 0.76)	-5.5 ( $\pm$ 1.15)	-4.8 ( $\pm$ 0.81)
Day 7	-7.2 ( $\pm$ 1.17)	-9.1 ( $\pm$ 1.09)	-9.3 ( $\pm$ 1.67)	-7.1 ( $\pm$ 1.16)
Day 14	-9.9 ( $\pm$ 1.31)	-12.5 ( $\pm$ 1.19)	-12.4 ( $\pm$ 1.8)	-10.7 ( $\pm$ 1.28)
Day 21	-12 ( $\pm$ 1.55)	-14.8 ( $\pm$ 1.4)	-15.2 ( $\pm$ 2.09)	-13.2 ( $\pm$ 1.5)
Day 28	-12.3 ( $\pm$ 1.69)	-17.1 ( $\pm$ 1.49)	-17.3 ( $\pm$ 2.21)	-15.5 ( $\pm$ 1.61)
Day 35	-17 ( $\pm$ 1.66)	-19 ( $\pm$ 1.48)	-20.3 ( $\pm$ 2.19)	-15.4 ( $\pm$ 1.58)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4849 <sup>[15]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	2.9
Variability estimate	Standard error of the mean
Dispersion value	1.09

Notes:

[15] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8902 <sup>[16]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	1.06

**Notes:**

[16] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5826 <sup>[17]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	1.36

**Notes:**

[17] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9271 <sup>[18]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	3
Variability estimate	Standard error of the mean
Dispersion value	1.61

Notes:

[18] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1902 <sup>[19]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	1.56

Notes:

[19] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.271 <sup>[20]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	2

Notes:

[20] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6773 <sup>[21]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	4.3
Variability estimate	Standard error of the mean
Dispersion value	1.79

Notes:

[21] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2895 <sup>[22]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1.72

Notes:

[22] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4261 <sup>[23]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	2.18

Notes:

[23] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5505 <sup>[24]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	5.5
Variability estimate	Standard error of the mean
Dispersion value	2.13

Notes:

[24] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4286 <sup>[25]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	2.03

Notes:

[25] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4423 <sup>[26]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	3.1
Variability estimate	Standard error of the mean
Dispersion value	2.56

Notes:

[26] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1691 <sup>[27]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	7.7
Variability estimate	Standard error of the mean
Dispersion value	2.3

Notes:

[27] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4682 <sup>[28]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	2.17

Notes:

[28] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4961 <sup>[29]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	3.5
Variability estimate	Standard error of the mean
Dispersion value	2.71

Notes:

[29] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4697 <sup>[30]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	2.8
Variability estimate	Standard error of the mean
Dispersion value	2.26

Notes:

[30] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0947 <sup>[31]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	2.14

Notes:

[31] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0675 <sup>[32]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	2.68

Notes:

[32] - Unadjusted p-value

### Secondary: Percentage of Participants Who Are PANSS Responders (≥30% Reduction From Baseline in PANSS Total Score) at Days 4, 7, 14, 21, 28 and 35

End point title	Percentage of Participants Who Are PANSS Responders (≥30% Reduction From Baseline in PANSS Total Score) at Days 4, 7, 14, 21, 28 and 35
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End point description:

A PANSS responder was defined as a participant who had a reduction from baseline of at least 30% in the PANSS total score at a post-baseline assessment. The PANSS is a 30-item clinician-rated instrument for assessing schizophrenia symptoms. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The Total score is the sum of the ratings for the individual items, and ranged from 30 to 210 with a higher score indicating greater severity of symptoms. Missing data were imputed by LOCF. Population for this analysis was FAS, defined as randomized participants who received ≥1 dose of study drug and had both a baseline and ≥1 post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Days 4, 7, 14, 21, 28 and 35

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: percentage of participants				
number (not applicable)				
Day 4 (n = 95,108,44,97)	0	0	0	2.1
Day 7 (n = 96,111,45,99)	2.1	5.4	0	5.1
Day 14 (n = 96,111,45,99)	5.2	5.4	4.4	7.1
Day 21 (n = 96,111,45,99)	8.3	14.4	11.1	13.1
Day 28 (n = 96,111,45,99)	10.4	16.2	15.6	14.1
Day 35 (n = 96,111,45,99)	15.6	21.6	15.6	17.2

### Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1736 <sup>[33]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[33] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1736 <sup>[34]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[34] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.285 <sup>[35]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[35] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.329 <sup>[36]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[36] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6938 <sup>[37]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[37] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1105 <sup>[38]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[38] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6804 <sup>[39]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[39] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9704 <sup>[40]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[40] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6604 <sup>[41]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[41] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Asenapine 2.5 mg BID v Placebo BID

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2447 <sup>[42]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[42] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4834 <sup>[43]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[43] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9189 <sup>[44]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[44] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.437 <sup>[45]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[45] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2894 <sup>[46]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[46] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6953 <sup>[47]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[47] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4892 <sup>[48]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[48] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1954 <sup>[49]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[49] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.799 <sup>[50]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[50] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

## Secondary: Change From Baseline in CGI-S Score at Days 4, 7, 14, 21, 28 and 35

End point title	Change From Baseline in CGI-S Score at Days 4, 7, 14, 21, 28 and 35
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End point description:

CGI-S is a 7-point scale for assessing the global severity of the participant's illness, with ratings from 1=normal, not ill to 7=very severely ill. The reported measure is the change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28 and 35

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-0.1 (± 0.05)	-0.2 (± 0.05)	-0.2 (± 0.07)	-0.2 (± 0.05)
Day 7	-0.3 (± 0.07)	-0.3 (± 0.06)	-0.3 (± 0.1)	-0.3 (± 0.07)
Day 14	-0.6 (± 0.08)	-0.6 (± 0.07)	-0.6 (± 0.11)	-0.5 (± 0.08)
Day 21	-0.6 (± 0.1)	-0.8 (± 0.09)	-0.8 (± 0.13)	-0.7 (± 0.09)
Day 28	-0.7 (± 0.11)	-0.9 (± 0.09)	-0.8 (± 0.14)	-0.8 (± 0.1)
Day 35	-0.9 (± 0.11)	-1.1 (± 0.1)	-1 (± 0.14)	-0.8 (± 0.1)

## Statistical analyses

Statistical analysis title	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4255 <sup>[51]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.07

Notes:

[51] - Unadjusted p-value

Statistical analysis title	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9564 <sup>[52]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.06

Notes:

[52] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6363 <sup>[53]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[53] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8759 <sup>[54]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[54] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9598 <sup>[55]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[55] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9789 <sup>[56]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[56] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4671 <sup>[57]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[57] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6359 <sup>[58]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[58] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5454 <sup>[59]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[59] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4188 <sup>[60]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[60] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5318 <sup>[61]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[61] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5683 <sup>[62]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[62] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2972 <sup>[63]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[63] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.482 <sup>[64]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[64] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9901 <sup>[65]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[65] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6682 <sup>[66]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[66] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1111 <sup>[67]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[67] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.24 <sup>[68]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[68] - Unadjusted p-value

### Secondary: Percentage of Participants Who Are Clinical Global Impression Scale-Improvement (CGI-I) Responders at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Percentage of Participants Who Are Clinical Global Impression Scale-Improvement (CGI-I) Responders at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

A CGI-I responder was defined as a participant who had a CGI-I score of 1 (very much improved) or 2 (much improved) at a post-baseline assessment. CGI-I is a 7-point scale for assessing the global improvement of the participant's illness relative to baseline, with ratings from 1=very much improved to 7=very much worse. Missing data were imputed by LOCF. Population for this analysis was FAS, defined as randomized participants who received ≥1 dose of study drug and had both a baseline and ≥1 post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: percentage of participants				
number (not applicable)				
Day 4 (n = 95,108,44,98)	34.7	33.3	43.2	37.8
Day 7 (n = 96,111,45,99)	51	46.8	60	45.5
Day 14 (n = 96,111,45,99)	51	60.4	71.1	54.5
Day 21 (n = 96,111,45,99)	54.2	63.1	75.6	58.6
Day 28 (n = 96,111,45,99)	58.3	62.2	73.3	60.6
Day 35 (n = 96,111,45,99)	60.4	64	82.2	64.6
Day 42 (n = 96,111,45,99)	59.4	66.7	84.4	62.6

### Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6205 <sup>[69]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[69] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4829 <sup>[70]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[70] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3945 <sup>[71]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[71] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4076 <sup>[72]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[72] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.969 <sup>[73]</sup>
Method	Cochran-Mantel-Haenszel



Notes:

[73] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.117 <sup>[74]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[74] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5088 <sup>[75]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[75] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3426 <sup>[76]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[76] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0762 <sup>[77]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[77] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Asenapine 2.5 mg BID v Placebo BID

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5531 <sup>[78]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[78] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4875 <sup>[79]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[79] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0692 <sup>[80]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[80] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7482 <sup>[81]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[81] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8037 <sup>[82]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[82] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0859 <sup>[83]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[83] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.585 <sup>[84]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[84] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9698 <sup>[85]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[85] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0132 <sup>[86]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[86] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7129 <sup>[87]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[87] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5074 [88]
Method	Cochran-Mantel-Haenszel

Notes:

[88] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004 [89]
Method	Cochran-Mantel-Haenszel

Notes:

[89] - P-value from Cochran Mantel-Haenszel test with an adjustment for pooled center

## **Secondary: Change From Baseline in PANSS Negative Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42**

End point title	Change From Baseline in PANSS Negative Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 7 items of the negative subscale of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Negative symptoms represent a diminution or loss of normal functions (e.g., emotional withdrawal). For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS negative subscale score for each participant was sum of the rating assigned to each of the 7 subscale items, and ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-0.7 ( $\pm$ 0.29)	-0.5 ( $\pm$ 0.27)	-0.9 ( $\pm$ 0.42)	-0.8 ( $\pm$ 0.29)
Day 7	-1.2 ( $\pm$ 0.33)	-1.3 ( $\pm$ 0.31)	-1.5 ( $\pm$ 0.47)	-1.1 ( $\pm$ 0.33)
Day 14	-1.6 ( $\pm$ 0.37)	-2.3 ( $\pm$ 0.34)	-1.7 ( $\pm$ 0.51)	-1.8 ( $\pm$ 0.37)

Day 21	-2.3 (± 0.41)	-2.5 (± 0.37)	-2 (± 0.56)	-2.3 (± 0.4)
Day 28	-2.5 (± 0.45)	-3.1 (± 0.4)	-2.6 (± 0.59)	-3 (± 0.43)
Day 35	-3.3 (± 0.48)	-3.4 (± 0.43)	-3.4 (± 0.63)	-2.6 (± 0.46)
Day 42	-3.3 (± 0.54)	-4.3 (± 0.48)	-3.8 (± 0.68)	-3.2 (± 0.51)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8829 <sup>[90]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.4
Notes:	
[90] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5488 <sup>[91]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1

Variability estimate	Standard error of the mean
Dispersion value	0.39

Notes:

[91] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.783 <sup>[92]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[92] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.807 <sup>[93]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[93] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.528 <sup>[94]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44
Notes:	
[94] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4025 <sup>[95]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.57
Notes:	
[95] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6471 <sup>[96]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.51
Notes:	
[96] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2504 <sup>[97]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.49
Notes:	
[97] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this	



record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9223 <sup>[98]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[98] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8839 <sup>[99]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[99] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID

Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8077 <sup>[100]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[100] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6216 <sup>[101]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[101] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4248 <sup>[102]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.61

Notes:

[102] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7667 <sup>[103]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[103] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6282 <sup>[104]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[104] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.315 <sup>[105]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.65

Notes:

[105] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1908 <sup>[106]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.61

Notes:

[106] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3128 <sup>[107]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.77

Notes:

[107] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8812 <sup>[108]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[108] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1143 <sup>[109]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.69

Notes:

[109] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4418 <sup>[110]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.84

Notes:

[110] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Positive Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Positive Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 7 items of the positive subscale of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Positive symptoms refer to an excess or distortion of normal mental status (e.g., delusions). For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS positive subscale score for each participant was sum of the rating assigned to each of the 7 subscale items, and ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-1.2 ( $\pm$ 0.29)	-1.6 ( $\pm$ 0.28)	-2.3 ( $\pm$ 0.42)	-1.7 ( $\pm$ 0.3)
Day 7	-2.3 ( $\pm$ 0.39)	-2.8 ( $\pm$ 0.36)	-3.6 ( $\pm$ 0.55)	-2.6 ( $\pm$ 0.38)
Day 14	-3.4 ( $\pm$ 0.45)	-3.9 ( $\pm$ 0.4)	-4.4 ( $\pm$ 0.61)	-3.7 ( $\pm$ 0.43)
Day 21	-4 ( $\pm$ 0.52)	-5 ( $\pm$ 0.47)	-5.7 ( $\pm$ 0.7)	-4.5 ( $\pm$ 0.51)
Day 28	-4.1 ( $\pm$ 0.59)	-5.7 ( $\pm$ 0.52)	-6.2 ( $\pm$ 0.77)	-5 ( $\pm$ 0.56)
Day 35	-5.2 ( $\pm$ 0.6)	-6.3 ( $\pm$ 0.53)	-6.8 ( $\pm$ 0.78)	-5.5 ( $\pm$ 0.57)
Day 42	-5.6 ( $\pm$ 0.65)	-7.2 ( $\pm$ 0.57)	-7.5 ( $\pm$ 0.83)	-5.4 ( $\pm$ 0.61)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.216 <sup>[111]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.4
Notes:	
[111] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9494 <sup>[112]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.39
Notes:	
[112] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1834 <sup>[113]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.5

**Notes:**

[113] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6347 <sup>[114]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.53

**Notes:**

[114] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6917 <sup>[115]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[115] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1431 <sup>[116]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.66

Notes:

[116] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6267 <sup>[117]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.61

Notes:

[117] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.726 <sup>[118]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[118] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3326 <sup>[119]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.74

Notes:

[119] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4575 <sup>[120]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[120] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.493 <sup>[121]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[121] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1886 <sup>[122]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.86

Notes:

[122] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2643 <sup>[123]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2.5
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[123] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3516 <sup>[124]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.76

Notes:

[124] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
-------------------	-----------------------------------

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2068 <sup>[125]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.94

Notes:

[125] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7284 <sup>[126]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.82

Notes:

[126] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2698 <sup>[127]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.77

Notes:

[127] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.151 <sup>[128]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.96

Notes:

[128] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8039 <sup>[129]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.88

Notes:

[129] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0306 <sup>[130]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[130] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0406 <sup>[131]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	1.03

Notes:

[131] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS General Psychopathology Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS General Psychopathology Subscale Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 16 items of the general psychopathology subscale of the PANSS, which is a 30-item clinician-rated instrument used to assess the symptoms of schizophrenia. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS general psychopathology subscale score for each participant was calculated as the sum of the rating assigned to each of the 16 subscale items, and ranged from 16 to 112 with a higher score indicating greater severity of symptoms. The reported measure is the change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-2.2 ( $\pm$ 0.49)	-2.7 ( $\pm$ 0.46)	-2.5 ( $\pm$ 0.7)	-2.4 ( $\pm$ 0.49)
Day 7	-3.8 ( $\pm$ 0.69)	-4.9 ( $\pm$ 0.64)	-4.4 ( $\pm$ 0.98)	-3.6 ( $\pm$ 0.68)
Day 14	-5.1 ( $\pm$ 0.73)	-6.2 ( $\pm$ 0.66)	-6.4 ( $\pm$ 1)	-5.4 ( $\pm$ 0.71)
Day 21	-5.9 ( $\pm$ 0.84)	-7.4 ( $\pm$ 0.76)	-7.7 ( $\pm$ 1.13)	-6.7 ( $\pm$ 0.81)
Day 28	-5.9 ( $\pm$ 0.93)	-8.2 ( $\pm$ 0.82)	-8.6 ( $\pm$ 1.21)	-7.7 ( $\pm$ 0.88)
Day 35	-8.8 ( $\pm$ 0.88)	-9.2 ( $\pm$ 0.79)	-10.2 ( $\pm$ 1.16)	-7.6 ( $\pm$ 0.84)
Day 42	-8.9 ( $\pm$ 0.97)	-10.1 ( $\pm$ 0.86)	-10.4 ( $\pm$ 1.23)	-8 ( $\pm$ 0.92)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7819 <sup>[132]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.66
Notes: [132] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.703 <sup>[133]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.65
Notes: [133] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.952 <sup>[134]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.83

**Notes:**

[134] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7907 <sup>[135]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.95

**Notes:**

[135] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1391 <sup>[136]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.91

Notes:

[136] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4901 <sup>[137]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	1.18

Notes:

[137] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8079 <sup>[138]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	2.2
Variability estimate	Standard error of the mean
Dispersion value	1

Notes:

[138] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3889 <sup>[139]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.95

Notes:

[139] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3907 <sup>[140]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	1.21

Notes:

[140] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5363 <sup>[141]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	3
Variability estimate	Standard error of the mean
Dispersion value	1.15

Notes:

[141] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5075 <sup>[142]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	1.09

Notes:

[142] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4526 <sup>[143]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	1.38

Notes:

[143] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1548 <sup>[144]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4.3
Variability estimate	Standard error of the mean
Dispersion value	1.26

Notes:

[144] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6589 <sup>[145]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	1.19

Notes:

[145] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5171 <sup>[146]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	1.48

Notes:

[146] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3133 <sup>[147]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[147] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1723 <sup>[148]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	1.13

Notes:

[148] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0663 <sup>[149]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	1.42

Notes:

[149] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5128 <sup>[150]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	1.32

Notes:

[150] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0842 <sup>[151]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	1.24

Notes:

[151] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1217 <sup>[152]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	1.52

Notes:

[152] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Marder Factor Positive Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Marder Factor Positive Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 8 items of the Marder positive symptom factor of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Marder factors are a modified grouping of the 30 PANSS items. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS Marder factor positive symptom score for each participant was sum of rating assigned to each of the 8 applicable Marder factor items, and ranged from 8 to 56 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-1.3 ( $\pm$ 0.29)	-1.8 ( $\pm$ 0.27)	-2 ( $\pm$ 0.41)	-2 ( $\pm$ 0.29)
Day 7	-2.5 ( $\pm$ 0.41)	-2.9 ( $\pm$ 0.38)	-3.2 ( $\pm$ 0.58)	-2.8 ( $\pm$ 0.4)
Day 14	-3.9 ( $\pm$ 0.49)	-4 ( $\pm$ 0.44)	-4.4 ( $\pm$ 0.67)	-4.1 ( $\pm$ 0.47)
Day 21	-4.5 ( $\pm$ 0.55)	-5.4 ( $\pm$ 0.5)	-5.5 ( $\pm$ 0.74)	-5.1 ( $\pm$ 0.54)
Day 28	-4.8 ( $\pm$ 0.6)	-6.3 ( $\pm$ 0.53)	-6.6 ( $\pm$ 0.78)	-5.6 ( $\pm$ 0.57)
Day 35	-6.1 ( $\pm$ 0.64)	-6.7 ( $\pm$ 0.57)	-6.9 ( $\pm$ 0.84)	-6.1 ( $\pm$ 0.61)
Day 42	-6.8 ( $\pm$ 0.67)	-7.6 ( $\pm$ 0.59)	-7.8 ( $\pm$ 0.86)	-6.2 ( $\pm$ 0.63)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0584 <sup>[153]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.39
Notes:	
[153] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5197 <sup>[154]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.38
Notes:	
[154] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9693 <sup>[155]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.49

**Notes:**

[155] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6161 <sup>[156]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.56

**Notes:**

[156] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.788 <sup>[157]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[157] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5526 <sup>[158]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[158] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7647 <sup>[159]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.67

Notes:

[159] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.89 <sup>[160]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.64

Notes:

[160] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7097 <sup>[161]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.81

Notes:

[161] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4601 <sup>[162]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.76

Notes:

[162] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6288 <sup>[163]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[163] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6099 <sup>[164]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.91

Notes:

[164] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.279 <sup>[165]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2.5
Variability estimate	Standard error of the mean
Dispersion value	0.82

Notes:

[165] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4253 <sup>[166]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.77

Notes:

[166] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3014 <sup>[167]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.96

Notes:

[167] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.972 <sup>[168]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.87

Notes:

[168] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4758 <sup>[169]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.82

Notes:

[169] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4419 <sup>[170]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	1.03

Notes:

[170] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
-------------------	------------------------------------

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4762 <sup>[171]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.91

Notes:

[171] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1046 <sup>[172]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.86

Notes:

[172] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1411 <sup>[173]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	1.06

Notes:

[173] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Marder Factor Negative Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Marder Factor Negative Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 7 items of the Marder negative symptoms factor of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Marder factors are a modified grouping of the 30 PANSS items. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS Marder factor negative symptom score for each participant was sum of the rating assigned to each of the 7 applicable Marder factor items, and ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-1.2 ( $\pm$ 0.3)	-0.8 ( $\pm$ 0.28)	-0.8 ( $\pm$ 0.43)	-0.7 ( $\pm$ 0.3)
Day 7	-1.7 ( $\pm$ 0.37)	-1.9 ( $\pm$ 0.34)	-1.8 ( $\pm$ 0.53)	-1.3 ( $\pm$ 0.37)
Day 14	-2 ( $\pm$ 0.41)	-2.8 ( $\pm$ 0.37)	-2.2 ( $\pm$ 0.56)	-2 ( $\pm$ 0.4)
Day 21	-2.6 ( $\pm$ 0.44)	-3.2 ( $\pm$ 0.4)	-2.6 ( $\pm$ 0.6)	-2.5 ( $\pm$ 0.43)
Day 28	-2.9 ( $\pm$ 0.51)	-3.8 ( $\pm$ 0.45)	-3.2 ( $\pm$ 0.67)	-3.5 ( $\pm$ 0.49)
Day 35	-3.5 ( $\pm$ 0.52)	-3.9 ( $\pm$ 0.46)	-4.1 ( $\pm$ 0.68)	-3 ( $\pm$ 0.49)
Day 42	-3.4 ( $\pm$ 0.53)	-4.7 ( $\pm$ 0.47)	-4.3 ( $\pm$ 0.67)	-4 ( $\pm$ 0.51)



## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2754 <sup>[174]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.4
Notes:	
[174] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.85 <sup>[175]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.39
Notes:	
[175] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8439 <sup>[176]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.51

**Notes:**

[176] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4741 <sup>[177]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.51

**Notes:**

[177] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2158 <sup>[178]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[178] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.506 <sup>[179]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.63

Notes:

[179] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9956 <sup>[180]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[180] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1624 <sup>[181]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.53

Notes:

[181] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7662 <sup>[182]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[182] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8363 <sup>[183]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.61

Notes:

[183] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2388 <sup>[184]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[184] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9435 <sup>[185]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[185] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4267 <sup>[186]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[186] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.681 <sup>[187]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.65

Notes:

[187] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7673 <sup>[188]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.82

Notes:

[188] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.483 <sup>[189]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[189] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2128 <sup>[190]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.66

Notes:

[190] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1756 <sup>[191]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[191] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4246 <sup>[192]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.72

Notes:

[192] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2873 <sup>[193]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[193] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7308 <sup>[194]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[194] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Marder Factor Disorganized Thought Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Marder Factor Disorganized Thought Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 7 items of the Marder disorganized thoughts factor of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Marder factors are a modified grouping of the 30 PANSS items. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS Marder factor disorganized thought symptom score for each participant was sum of rating assigned to each of the 7 applicable Marder factor items, and ranged from 7 to 49 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received ≥1 dose of study drug and had both a baseline and ≥1 post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-0.3 (± 0.24)	-0.7 (± 0.22)	-1.1 (± 0.34)	-0.7 (± 0.24)
Day 7	-1 (± 0.32)	-1.4 (± 0.29)	-1.6 (± 0.45)	-0.7 (± 0.31)
Day 14	-1.3 (± 0.36)	-2 (± 0.33)	-2.2 (± 0.49)	-1.5 (± 0.35)
Day 21	-2.3 (± 0.41)	-2.5 (± 0.37)	-2.7 (± 0.54)	-2.1 (± 0.39)
Day 28	-2.4 (± 0.42)	-3.1 (± 0.37)	-3.1 (± 0.54)	-2.4 (± 0.4)
Day 35	-3.5 (± 0.43)	-3.5 (± 0.38)	-4.3 (± 0.56)	-2.4 (± 0.41)
Day 42	-3.8 (± 0.45)	-4.3 (± 0.4)	-4.7 (± 0.58)	-2.7 (± 0.43)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2116 <sup>[195]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.32
Notes: [195] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9039 <sup>[196]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.31
Notes: [196] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2959 <sup>[197]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.4

**Notes:**

[197] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5909 <sup>[198]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44

**Notes:**

[198] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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**Statistical analysis description:**

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1489 <sup>[199]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[199] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1 <sup>[200]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[200] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.783 <sup>[201]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[201] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2679 <sup>[202]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[202] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2321 <sup>[203]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[203] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7368 <sup>[204]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[204] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4606 <sup>[205]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.53

Notes:

[205] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3241 <sup>[206]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.66

Notes:

[206] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
-------------------	------------------------------------

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.986 <sup>[207]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[207] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.189 <sup>[208]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.53

Notes:

[208] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
-------------------	-----------------------------------

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.303 <sup>[209]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.67

Notes:

[209] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.055 <sup>[210]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[210] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
-------------------	----------------------------------

Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0415 <sup>[211]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[211] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0058 <sup>[212]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.69

Notes:

[212] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
-------------------	------------------------------------

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0691 <sup>[213]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[213] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0063 <sup>[214]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[214] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0056 <sup>[215]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.71

Notes:

[215] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Marder Factor Hostility/Excitement Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Marder Factor Hostility/Excitement Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 4 items of the Marder hostility/excitement factor of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Marder factors are a modified grouping of the 30 PANSS items. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS Marder factor hostility/excitement symptom score for each participant was sum of rating assigned to each of the 4 applicable Marder factor items, and ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-0.4 ( $\pm$ 0.25)	-0.3 ( $\pm$ 0.23)	-0.7 ( $\pm$ 0.36)	-0.5 ( $\pm$ 0.25)
Day 7	-0.5 ( $\pm$ 0.28)	-0.5 ( $\pm$ 0.26)	-1 ( $\pm$ 0.4)	-0.7 ( $\pm$ 0.28)
Day 14	-0.9 ( $\pm$ 0.3)	-0.8 ( $\pm$ 0.27)	-1.2 ( $\pm$ 0.41)	-0.9 ( $\pm$ 0.3)
Day 21	-0.8 ( $\pm$ 0.33)	-0.9 ( $\pm$ 0.3)	-1.8 ( $\pm$ 0.44)	-1 ( $\pm$ 0.32)
Day 28	-0.5 ( $\pm$ 0.41)	-0.8 ( $\pm$ 0.36)	-1.6 ( $\pm$ 0.53)	-1 ( $\pm$ 0.39)
Day 35	-1.4 ( $\pm$ 0.37)	-1.5 ( $\pm$ 0.32)	-2 ( $\pm$ 0.47)	-1.4 ( $\pm$ 0.35)
Day 42	-1.1 ( $\pm$ 0.41)	-1.8 ( $\pm$ 0.36)	-1.9 ( $\pm$ 0.52)	-1.1 ( $\pm$ 0.39)

## Statistical analyses

Statistical analysis title	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7847 <sup>[216]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.34
Notes:	
[216] - Unadjusted p-value	

Statistical analysis title	Comparison by Treatment Group: Day 4
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5859 <sup>[217]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.8

Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[217] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6413 <sup>[218]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.43

Notes:

[218] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7307 <sup>[219]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.38



Notes:

[219] - Unadjusted p-value

Statistical analysis title	Comparison by Treatment Group: Day 7
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7176 <sup>[220]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.37
Notes:	
[220] - Unadjusted p-value	

Statistical analysis title	Comparison by Treatment Group: Day 7
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.486 <sup>[221]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.48
Notes:	
[221] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9321 <sup>[222]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.41
Notes:	
[222] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7691 <sup>[223]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.39
Notes:	
[223] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this	

record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5694 <sup>[224]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[224] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5583 <sup>[225]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[225] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID

Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7307 <sup>[226]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.43

Notes:

[226] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1715 <sup>[227]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[227] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4219 <sup>[228]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[228] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7437 <sup>[229]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[229] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.311 <sup>[230]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.65

Notes:

[230] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9805 <sup>[231]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[231] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8741 <sup>[232]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[232] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3288 <sup>[233]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[233] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9336 <sup>[234]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[234] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1722 <sup>[235]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[235] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1909 <sup>[236]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.64

Notes:

[236] - Unadjusted p-value

### Secondary: Change From Baseline in PANSS Marder Factor Anxiety/Depression Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42

End point title	Change From Baseline in PANSS Marder Factor Anxiety/Depression Symptom Score at Days 4, 7, 14, 21, 28, 35 and 42
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End point description:

This measure reports results for the 4 items of the Marder anxiety/depression factor of the PANSS, which is a 30-item clinician-rated instrument used to assess schizophrenia symptoms. Marder factors are a modified grouping of the 30 PANSS items. For each item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. PANSS Marder factor anxiety/depression symptom score for each participant was sum of rating assigned to each of the 4 applicable Marder factor items, and ranged from 4 to 28 with a higher score indicating greater severity of symptoms. Measure reports change from baseline; improvement in symptoms is represented by negative values. Population for this analysis was FAS, defined as randomized participants who received  $\geq 1$  dose of study drug and had both a baseline and  $\geq 1$  post-baseline PANSS Total Score.

End point type	Secondary
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End point timeframe:

Baseline and Days 4, 7, 14, 21, 28, 35 and 42

End point values	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD	Placebo BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	111	45	99
Units: score on a scale				
least squares mean (standard error)				
Day 4	-0.9 ( $\pm$ 0.27)	-1.2 ( $\pm$ 0.25)	-1 ( $\pm$ 0.38)	-0.9 ( $\pm$ 0.27)
Day 7	-1.5 ( $\pm$ 0.3)	-2.2 ( $\pm$ 0.28)	-1.8 ( $\pm$ 0.43)	-1.7 ( $\pm$ 0.3)
Day 14	-1.9 ( $\pm$ 0.31)	-2.9 ( $\pm$ 0.28)	-2.5 ( $\pm$ 0.42)	-2.5 ( $\pm$ 0.3)
Day 21	-2.1 ( $\pm$ 0.32)	-3 ( $\pm$ 0.29)	-2.7 ( $\pm$ 0.42)	-3.1 ( $\pm$ 0.31)
Day 28	-1.9 ( $\pm$ 0.36)	-3.2 ( $\pm$ 0.32)	-2.8 ( $\pm$ 0.47)	-3.4 ( $\pm$ 0.35)
Day 35	-3 ( $\pm$ 0.34)	-3.6 ( $\pm$ 0.3)	-3.2 ( $\pm$ 0.44)	-3.2 ( $\pm$ 0.32)
Day 42	-2.9 ( $\pm$ 0.4)	-3.4 ( $\pm$ 0.35)	-3.1 ( $\pm$ 0.5)	-3 ( $\pm$ 0.38)

## Statistical analyses

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9851 [237]
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.37
Notes:	
[237] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4912 [238]
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5

Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[238] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 4
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8559 <sup>[239]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.46

Notes:

[239] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 7
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5635 <sup>[240]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[240] - Unadjusted p-value

Statistical analysis title	Comparison by Treatment Group: Day 7
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2321 <sup>[241]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.4
Notes:	
[241] - Unadjusted p-value	

Statistical analysis title	Comparison by Treatment Group: Day 7
Statistical analysis description: "Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8867 <sup>[242]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.52
Notes:	
[242] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1499 <sup>[243]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.42
Notes:	
[243] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.286 <sup>[244]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.4
Notes:	
[244] - Unadjusted p-value	

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 14
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this	

record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8978 <sup>[245]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[245] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0283 <sup>[246]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[246] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
Statistical analysis description:	
"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.	
Comparison groups	Asenapine 5 mg BID v Placebo BID

Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8667 <sup>[247]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[247] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 21
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5044 <sup>[248]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[248] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004 <sup>[249]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[249] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.633 <sup>[250]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.46

Notes:

[250] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 28
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2981 <sup>[251]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[251] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6556 <sup>[252]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[252] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2889 <sup>[253]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.43

Notes:

[253] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 35
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9399 <sup>[254]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.53

Notes:

[254] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 2.5 mg BID v Placebo BID
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Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8955 <sup>[255]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[255] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Asenapine 5 mg BID v Placebo BID
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3681 <sup>[256]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[256] - Unadjusted p-value

<b>Statistical analysis title</b>	Comparison by Treatment Group: Day 42
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Statistical analysis description:

"Number of subjects included in analysis" presented below is sum of participants in the FAS population in the 2 treatment groups compared and is automatically calculated by data entry system for this record; however, MMRM model used for analysis includes entire FAS population in all 4 treatment groups, which includes 351 participants.

Comparison groups	Olanzapine 15 mg QD v Placebo BID
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Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8215 <sup>[257]</sup>
Method	MMRM
Parameter estimate	LS means difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[257] - Unadjusted p-value

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 30 days after last dose of study drug (Up to approximately 10 weeks)

Adverse event reporting additional description:

Analysis population is all randomized participants who received  $\geq 1$  dose of study drug

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	Asenapine 2.5 mg BID
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Reporting group description:

Participants were administered one 2.5 mg asenapine tablet BID for 42 days

Reporting group title	Asenapine 5 mg BID
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Reporting group description:

Participants were administered one 5 mg asenapine tablet BID for 42 days

Reporting group title	Olanzapine 15 mg QD
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Reporting group description:

Participants were administered 15 mg olanzapine (as one 10 mg and one 5 mg tablet) QD for 42 days, except during Week 1 olanzapine 10 mg QD was administered

Reporting group title	Placebo BID
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Reporting group description:

Participants were administered placebo tablets BID for 42 days

Serious adverse events	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 97 (5.15%)	5 / 113 (4.42%)	1 / 46 (2.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Syncope			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 97 (0.00%)	1 / 113 (0.88%)	0 / 46 (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
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 97 (1.03%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 97 (0.00%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Homicidal ideation			
subjects affected / exposed	1 / 97 (1.03%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			

subjects affected / exposed	2 / 97 (2.06%)	0 / 113 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	0 / 97 (0.00%)	3 / 113 (2.65%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia, paranoid type			
subjects affected / exposed	0 / 97 (0.00%)	1 / 113 (0.88%)	0 / 46 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 97 (1.03%)	0 / 113 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Placebo BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 101 (7.92%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Homicidal ideation			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			



subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Schizophrenia, paranoid type			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 101 (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 %

<b>Non-serious adverse events</b>	Asenapine 2.5 mg BID	Asenapine 5 mg BID	Olanzapine 15 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 97 (27.84%)	47 / 113 (41.59%)	17 / 46 (36.96%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 97 (0.00%)	6 / 113 (5.31%)	0 / 46 (0.00%)
occurrences (all)	0	6	0
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 97 (10.31%)	10 / 113 (8.85%)	4 / 46 (8.70%)
occurrences (all)	12	10	6
Somnolence			
subjects affected / exposed	3 / 97 (3.09%)	7 / 113 (6.19%)	5 / 46 (10.87%)
occurrences (all)	3	7	5
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	0 / 97 (0.00%)	2 / 113 (1.77%)	3 / 46 (6.52%)
occurrences (all)	0	2	3
Dry mouth			
subjects affected / exposed	0 / 97 (0.00%)	2 / 113 (1.77%)	5 / 46 (10.87%)
occurrences (all)	0	2	5
Dyspepsia			
subjects affected / exposed	1 / 97 (1.03%)	2 / 113 (1.77%)	3 / 46 (6.52%)
occurrences (all)	1	2	3
Hypoaesthesia oral			
subjects affected / exposed	4 / 97 (4.12%)	7 / 113 (6.19%)	0 / 46 (0.00%)
occurrences (all)	4	7	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	3 / 97 (3.09%)	7 / 113 (6.19%)	0 / 46 (0.00%)
occurrences (all)	3	8	0
Anxiety			
subjects affected / exposed	7 / 97 (7.22%)	8 / 113 (7.08%)	4 / 46 (8.70%)
occurrences (all)	10	9	5
Insomnia			
subjects affected / exposed	9 / 97 (9.28%)	17 / 113 (15.04%)	4 / 46 (8.70%)
occurrences (all)	9	21	4
Schizophrenia			
subjects affected / exposed	6 / 97 (6.19%)	4 / 113 (3.54%)	0 / 46 (0.00%)
occurrences (all)	6	4	0

<b>Non-serious adverse events</b>	Placebo BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 101 (28.71%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 101 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences (all)	2		

Somnolence subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	2 / 101 (1.98%) 2		
Dry mouth subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	2 / 101 (1.98%) 2		
Hypoaesthesia oral subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0		
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	3 / 101 (2.97%) 3		
Anxiety subjects affected / exposed occurrences (all)	12 / 101 (11.88%) 13		
Insomnia subjects affected / exposed occurrences (all)	14 / 101 (13.86%) 20		
Schizophrenia subjects affected / exposed occurrences (all)	4 / 101 (3.96%) 4		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2012	Amendment 01: Primary reason for amendment was to incorporate revisions to eligibility criteria, drug packaging/labeling and dosing instructions, list of events requiring discontinuation of subject from trial, schedule of assessments and statistical analysis, and to remove text stating that a Data Safety Monitoring Board would participate in study. Original base protocol and Amendments 01 and 02 were submitted together to country authority (Croatia health ministry) that provided approval.
14 November 2012	Amendment 02: Primary reason for amendment was to incorporate revisions to medications/treatments prohibited prior to and during trial, safety assessments, list of events defined to be serious adverse events, list of closely monitored events and procedures for liver enzyme monitoring. Original base protocol and Amendments 01 and 02 were submitted together to country authority (Croatia health ministry) that provided approval.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported