EU Clinical Trials Register

Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Fixed-Dose, 6-Week, In-Patient Study to Assess Efficacy and Safety of HP-3070 in Subjects Diagnosed with Schizophrenia

Summary

EudraCT number	2015-005134-21
Trial protocol	SK
Global end of trial date	21 November 2017

Results information

Result version number	v2 (current)
This version publication date	14 March 2020
First version publication date	15 March 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	HP-3070-GL-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02876900
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Noven Pharmaceuticals, Inc.
Sponsor organisation address	100 Town Square Place, 5th Floor, Jersey City, New Jersey, United States, 07310
Public contact	Monica Lara, Noven Pharmaceuticals, Inc., +1 305 964 3569, mlara@noven.com
Scientific contact	George Harb, MD, MPH, Noven Pharmaceuticals, Inc., +1 551 233 2656, gharb@noven.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	21 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate efficacy of HP-3070 [asenapine transdermal patch] compared with placebo for the treatment of schizophrenia as evaluated by Positive and Negative Syndrome Scale (PANSS) total score.

Protection of trial subjects:

The study was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonisation Good Clinical Practice Guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 181
Country: Number of subjects enrolled	Serbia: 57
Country: Number of subjects enrolled	Ukraine: 106
Country: Number of subjects enrolled	United States: 185
Country: Number of subjects enrolled	Bulgaria: 88
Worldwide total number of subjects	617
EEA total number of subjects	88

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	607
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 59 centers across 5 countries between 22 Aug 2016 and 21 Nov 2017. Participants with a diagnosis of schizophrenia who were in an acute exacerbation, had a PANSS total score >=80 and Clinical Global Impression - Severity of Illness Scale (CGI-S) score >=4 were recruited.

Pre-assignment

Screening details:

This study consisted of a screening/run-in period of 3 to 14 days, followed by a 6-week double-blind treatment period and a 30-day follow-up period. A total of 617 participants were enrolled in the study and randomized to study treatment.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	High Dose Asenapine Maleate Transdermal Patch

Arm description:

Participants in the high dose asenapine maleate transdermal patch treatment arm received 2 asenapine maleate transdermal patches, once daily for 42 days.

Arm type	Experimental
Investigational medicinal product name	HP-3070-High Dose
Investigational medicinal product code	
Other name	asenapine maleate
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

Two HP3070 patches with each patch containing asenapine maleate consisting of a plastic film, adhesive matrix, and backing film.

Arm title	Low Dose Asenapine Maleate Transdermal Patch

Arm description:

Participants in the low dose asenapine maleate transdermal patch treatment arm received 1 asenapine maleate transdermal patch and 1 placebo (matching with HP-3070) transdermal patch, once daily for 42 days.

Arm type	Experimental
Investigational medicinal product name	HP-3070-Low Dose
Investigational medicinal product code	
Other name	asenapine maleate
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

One HP3070 patch containing asenapine maleate consisting of a plastic film, adhesive matrix, and backing film.

Investigational medicinal product name	HP-3070 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch

Routes of administration	Transdermal use

Dosage and administration details:

One HP3070 Placebo patch containing 0.0 mg asenapine maleate consisting of a plastic film, adhesive matrix, and backing film.

Arm title	Placebo

Arm description:

Participants in the Placebo arm received 2 placebo (matching with HP-3070) transdermal patches, once daily for 42 days.

Arm type	Placebo
Investigational medicinal product name	HP-3070 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

Two HP3070 Placebo patches with each patch containing 0.0 mg asenapine maleate consisting of a plastic film, adhesive matrix, and backing film.

Number of subjects in period 1	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo
Started	206	205	206
Received treatment	204	204	206
Completed	158	166	162
Not completed	48	39	44
Consent withdrawn by subject	18	20	14
Physician decision	-	1	2
Adverse event, non-fatal	16	10	14
Incorrectly randomised	-	1	-
Unspecified	3	3	1
Did not receive treatment	2	-	-
Lack of efficacy	8	4	12
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	High Dose Asenapine Maleate Transdermal Patch
Reporting group description:	
Participants in the high dose asenapine maleate transdermal patch treatment arm received 2 asenapine maleate transdermal patches, once daily for 42 days.	
Reporting group title	Low Dose Asenapine Maleate Transdermal Patch
Reporting group description:	
Participants in the low dose asenapine maleate transdermal patch treatment arm received 1 asenapine maleate transdermal patch and 1 placebo (matching with HP-3070) transdermal patch, once daily for 42 days.	
Reporting group title	Placebo
Reporting group description:	
Participants in the Placebo arm received 2 placebo (matching with HP-3070) transdermal patches, once daily for 42 days.	

Reporting group values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo
Number of subjects	206	205	206
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	200	203	204
From 65-84 years	6	2	2
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	95	74	75
Male	111	131	131

Reporting group values	Total		
Number of subjects	617		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	607		

From 65-84 years	10		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	244		
Male	373		

End points

End points reporting groups

Reporting group title	High Dose Asenapine Maleate Transdermal Patch
Reporting group description:	
Participants in the high dose asenapine maleate transdermal patch treatment arm received 2 asenapine maleate transdermal patches, once daily for 42 days.	
Reporting group title	Low Dose Asenapine Maleate Transdermal Patch
Reporting group description:	
Participants in the low dose asenapine maleate transdermal patch treatment arm received 1 asenapine maleate transdermal patch and 1 placebo (matching with HP-3070) transdermal patch, once daily for 42 days.	
Reporting group title	Placebo
Reporting group description:	
Participants in the Placebo arm received 2 placebo (matching with HP-3070) transdermal patches, once daily for 42 days.	

Primary: Change From Baseline in PANSS Total Score at Week 6

End point title	Change From Baseline in PANSS Total Score at Week 6
End point description:	
The PANSS total score is the sum of all 30 items (7 positive items, 7 negative items, and 16 general psychopathology items). For each item, severity was rated on an anchored 7-point scale, with a score of 1 indicating the absence of symptoms and a score of 7 indicating extremely severe symptoms. If one or more items are missing at a given assessment, the total score is set to missing. Baseline is defined as the last non-missing measurement taken prior to first dose of double-blind study medication. Results were presented for participants in the full analysis set (FAS) who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score).	
End point type	Primary
End point timeframe:	
Baseline (Day 0) and Week 6	

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	168	163	
Units: Units on a scale				
least squares mean (standard error)	-20.4 (± 1.162)	-22.1 (± 1.158)	-15.5 (± 1.166)	

Statistical analyses

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.003 [2]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.06
upper limit	-1.64
Variability estimate	Standard error of the mean
Dispersion value	1.634

Notes:

[1] - Assuming an effect size of 0.35 on the change in PANSS total score from baseline to Week 6 for the 2 pairwise comparisons between each active asenapine maleate transdermal patch treatment arm and placebo, the power for detecting a statistically significant HP-3070 advantage was approximately 0.90, having 204 evaluable participants per each treatment arm using a 2-sided alpha level of 0.025 for each comparison.

[2] - Adjusted p-value was calculated according to the truncated Hochberg procedure with a truncation factor y=0.9. Adjustment for multiple comparisons uses a parallel gatekeeping procedure.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001 [4]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.81
upper limit	-3.4
Variability estimate	Standard error of the mean
Dispersion value	1.63

Notes:

[3] - Assuming an effect size of 0.35 on the change in PANSS total score from baseline to Week 6 for the 2 pairwise comparisons between each active asenapine maleate transdermal patch treatment arm and placebo, the power for detecting a statistically significant HP-3070 advantage was approximately 0.90, having 204 evaluable participants per each treatment arm using a 2-sided alpha level of 0.025 for each comparison.

[4] - Adjusted p-value was calculated according to the truncated Hochberg procedure with a truncation factor γ=0.9. Adjustment for multiple comparisons uses a parallel gatekeeping procedure.

Secondary: Change From Baseline in CGI-S Scores at Week 6

End point title	Change From Baseline in CGI-S Scores at Week 6

End point description:

The severity of illness for each participant was rated using the CGI-S. The rater or Investigator answered the following question: "Considering your total clinical experience with this particular population, how mentally ill is the participant at this time?". Response choices included: 0 = not assessed; 1 = normal, not at all ill, 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; and 7 = among the most extremely ill participants. Baseline is defined as the last non-missing measurement taken prior to first dose of double-blind study medication. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score).

End point type	Secondary

End point timeframe:

Baseline (Day 0) and Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	168	164	
Units: Units on a scale				
least squares mean (standard error)	-1.1 (± 0.071)	-1.2 (± 0.071)	-0.8 (± 0.071)	

Statistical analyses

Statistical analysis title	Treatment Comparison CGI-S at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[5] - Adjusted p-value was calculated according to the Hochberg procedure. Adjustment for multiple comparisons uses a parallel gatekeeping procedure.

Statistical analysis title	Treatment Comparison CGI-S at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.099

Notes:

[6] - Adjusted p-value was calculated according to the Hochberg procedure. Adjustment for multiple comparisons uses a parallel gatekeeping procedure.

Secondary: Change From Baseline in PANSS Total Score at Each Time Point in Addition to Week 6

End point title	Change From Baseline in PANSS Total Score at Each Time Point in Addition to Week 6

End point description:

The PANSS total score is the sum of all 30 items (7 positive items, 7 negative items, and 16 general psychopathology items). For each item, severity was rated on an anchored 7-point scale, with a score of 1 indicating the absence of symptoms and a score of 7 indicating extremely severe symptoms. If one or more items are missing at a given assessment, the total score is set to missing. Baseline is defined as the last non-missing measurement taken prior to first dose of double-blind study medication. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0) through Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	201	
Units: Units on a scale				
least squares mean (standard error)				
Change from baseline at Week 1 (n=203, 201, 201)	-5.7 (± 0.558)	-5.5 (± 0.559)	-4.8 (± 0.560)	
Change from baseline at Week 2 (n=194, 196, 193)	-10.3 (± 0.741)	-10.9 (± 0.739)	-8.3 (± 0.742)	
Change from baseline at Week 3 (n=188, 186, 185)	-13.5 (± 0.860)	-13.9 (± 0.861)	-10.9 (± 0.863)	
Change from baseline at Week 4 (n=182, 180, 179)	-16.0 (± 0.963)	-18.1 (± 0.963)	-13.3 (± 0.967)	
Change from baseline at Week 5 (n=174, 178, 174)	-18.3 (± 1.073)	-20.5 (± 1.071)	-14.5 (± 1.077)	
Change from baseline at Week 6 (n=164, 168, 165)	-20.4 (± 1.159)	-22.1 (± 1.155)	-15.6 (± 1.163)	

Statistical analyses

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.226
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	0.764

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.332
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	0.76
Variability estimate	Standard error of the mean
Dispersion value	0.764

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.052
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.02
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	1.028

Notes:

[7] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.013
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.57
upper limit	-0.53
Variability estimate	Standard error of the mean
Dispersion value	1.026

Notes:

[8] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.036
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.89
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	1.202

Notes:

[9] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.013
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.36
upper limit	-0.64
Variability estimate	Standard error of the mean
Dispersion value	1.201

Notes:

[10] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.05
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.31
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	1.35

Notes:

[11] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.46
upper limit	-2.16
Variability estimate	Standard error of the mean
Dispersion value	1.349

Notes:

[12] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.012
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.77
upper limit	-0.84
Variability estimate	Standard error of the mean
Dispersion value	1.507

Notes:

[13] - Subjects in this analysis = 348.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.96
upper limit	-3.05
Variability estimate	Standard error of the mean
Dispersion value	1.505

Notes:

[14] - Subjects in this analysis = 352.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.003
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.99
upper limit	-1.59
Variability estimate	Standard error of the mean
Dispersion value	1.63

Notes:

[15] - Subjects in this analysis = 329.

Statistical analysis title	Treatment Comparison PANSS Total Score at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.74
upper limit	-3.35
Variability estimate	Standard error of the mean
Dispersion value	1.626

Notes:

[16] - Subjects in this analysis = 333.

Secondary: Change From Baseline in CGI-S at Each Time Point in Addition to Week 6

End point title	Change From Baseline in CGI-S at Each Time Point in Addition to Week 6

End point description:

The severity of illness for each participant was rated using CGI-S. The rater or Investigator answered following question: "Considering your total clinical experience with this particular population, how mentally ill is the participant at this time?". Response choices included: 0 = not assessed; 1 = normal, not at all ill, 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; and 7 = among the most extremely ill participants. Baseline is defined as last non-missing measurement taken prior to first dose of double-blind study medication. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0) through Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	200	201	
Units: Units on a scale				
least squares mean (standard error)				
Change from baseline at Week 1 (n=203, 200, 201)	-0.2 (± 0.034)	-0.2 (± 0.034)	-0.1 (± 0.034)	
Change from baseline at Week 2 (n=194, 196, 193)	-0.5 (± 0.047)	-0.5 (± 0.047)	-0.3 (± 0.047)	
Change from baseline at Week 3 (n=188, 186, 185)	-0.8 (± 0.056)	-0.7 (± 0.056)	-0.5 (± 0.056)	
Change from baseline at Week 4 (n=182, 180, 179)	-0.9 (± 0.062)	-1.0 (± 0.062)	-0.6 (± 0.062)	
Change from baseline at Week 5 (n=174, 178, 173)	-1.1 (± 0.064)	-1.1 (± 0.064)	-0.7 (± 0.065)	

Change from baseline at Week 6 (n=164, 168, 164)	-1.1 (± 0.071)	-1.2 (± 0.071)	-0.8 (± 0.071)	

Statistical analyses

Statistical analysis title	Treatment Comparison CGI-S at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.046

Statistical analysis title	Treatment Comparison CGI-S at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.156
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.03

Variability estimate	Standard error of the mean
Dispersion value	0.047

Statistical analysis title	Treatment Comparison CGI-S at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.017
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.066

Notes:

[17] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison CGI-S at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.002
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.066

Notes:

[18] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison CGI-S at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.002
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.078

Notes:

[19] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison CGI-S at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.005
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.079

Notes:

[20] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison CGI-S at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.087

Notes:

[21] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison CGI-S at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.087

Notes:

[22] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison CGI-S at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of

repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[23] - Subjects in this analysis = 347.

Statistical analysis title	Treatment Comparison CGI-S at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[24] - Subjects in this analysis = 351.

Statistical analysis title	Treatment Comparison CGI-S at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[25] - Subjects in this analysis = 328.

Statistical analysis title	Treatment Comparison CGI-S at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.099

Notes:

[26] - Subjects in this analysis = 332.

Secondary: Clinical Global Impression - Improvement Scale (CGI-I) Score at Each Time Point

End point title	Clinical Global Impression - Improvement Scale (CGI-I) Score at Each Time Point

End point description:

The efficacy of study medication was rated for each participant using the CGI-I. The rater or Investigator rated whether or not the participant's total improvement was due entirely to drug treatment. All responses were compared with the participant's condition at baseline prior to the first dose of double-blind study medication. Response choices included: 0 = not assessed, 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline

assessment of the primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Up to Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	201	
Units: Units on a scale				
arithmetic mean (standard deviation)				
At Week 1 (n=203, 201, 201)	3.6 (± 0.68)	3.6 (± 0.66)	3.7 (± 0.69)	
At Week 2 (n=194, 196, 193)	3.3 (± 0.86)	3.3 (± 0.85)	3.5 (± 0.88)	
At Week 3 (n=188, 186, 185)	3.0 (± 0.89)	3.1 (± 0.86)	3.2 (± 1.03)	
At Week 4 (n=182, 180, 179)	2.9 (± 1.00)	2.7 (± 0.87)	3.1 (± 1.01)	
At Week 5 (n=174, 178, 173)	2.7 (± 0.95)	2.7 (± 0.94)	3.0 (± 1.06)	
At Week 6 (n=163, 168, 163)	2.6 (± 1.03)	2.5 (± 0.96)	2.8 (± 1.06)	

Statistical analyses

Statistical analysis title	Treatment Comparison CGI-I at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.355
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.091

Statistical analysis title	Treatment Comparison CGI-I at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.346
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.091

Statistical analysis title	Treatment Comparison CGI-I at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.055
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.093

Notes:

[27] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison CGI-I at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation

of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	= 0.02
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.092

Notes:

[28] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison CGI-I at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.035
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.094

Notes:

[29] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison CGI-I at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.144
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.094

Notes:

[30] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison CGI-I at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.008
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.094

Notes:

[31] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison CGI-I at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.095

Notes:

[32] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison CGI-I at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.095

Notes:

[33] - Subjects in this analysis = 347.

Statistical analysis title	Treatment Comparison CGI-I at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.095

Notes:

[34] - Subjects in this analysis = 351.

Statistical analysis title	Treatment Comparison CGI-I at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	= 0.005
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.097

Notes:

[35] - Subjects in this analysis = 326.

Statistical analysis title	Treatment Comparison CGI-I at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value of CGI-S as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.097

Notes:

[36] - Subjects in this analysis = 331.

Secondary: Percentage of CGI-I Responders at Each Time Point Including Week 6

End point title	Percentage of CGI-I Responders at Each Time Point Including Week 6

End point description:

The CGI-I responders are defined as participants who have a score of 1 (very much improved) or a score of 2 (much improved). Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score).

End point type	Secondary

End point timeframe:

Up to Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	203	
Units: Percentage of participants				
number (not applicable)				
At Week 1	4.4	4.0	3.4	
At Week 2	17.7	12.4	12.3	
At Week 3	27.1	20.4	21.2	
At Week 4	36.0	38.8	25.6	
At Week 5	42.9	46.3	29.1	
At Week 6	43.3	49.8	34.0	

Statistical analyses

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 1

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.61
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.127

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 1

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.803
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.131

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 2

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution.

95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.118
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.069

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 2

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.958
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.076

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 3

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.173
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.058

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 3

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.785
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.062

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 4

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.055

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 4

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.054

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 5

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.054

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 5

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.053

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 6

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.055

Statistical analysis title	Treatment Comparison CGI-I Responders at Week 6

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentage between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.054

Secondary: Change From Baseline in Positive, Negative, and General Pathology Subscores of PANSS at Each Time Point

End point title	Change From Baseline in Positive, Negative, and General Pathology Subscores of PANSS at Each Time Point

End point description:

The PANSS consists of 3 subscales containing a total of 30 items. For each item, severity was rated on an anchored 7-point scale, with a score of 1 indicating absence of symptoms and a score of 7 indicating extremely severe symptoms. The subscales were as follows: Positive subscale (PS; 7 items), Negative subscale (NS; 7 items), and General psychopathology subscale (GP; 16 items). Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0) through Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	201	
Units: Units on a scale				
arithmetic mean (standard deviation)				
PS: Change from baseline at Week 1 (n=203,201,201)	-1.8 (± 2.83)	-1.9 (± 2.60)	-1.6 (± 2.97)	
PS: Change from baseline at Week 2 (n=194,196,193)	-3.4 (± 3.68)	-3.8 (± 3.42)	-2.8 (± 3.65)	
PS: Change from baseline at Week 3 (n=188,186,185)	-4.8 (± 4.18)	-5.0 (± 3.62)	-4.1 (± 4.17)	
PS: Change from baseline at Week 4 (n=182,180,179)	-5.4 (± 4.76)	-6.1 (± 4.27)	-4.9 (± 4.46)	
PS: Change from baseline at Week 5 (n=174,178,174)	-6.5 (± 4.99)	-7.1 (± 4.62)	-5.5 (± 4.80)	
PS: Change from baseline at Week 6 (n=164,168,165)	-7.5 (± 5.04)	-7.7 (± 4.70)	-6.1 (± 4.94)	
NS: Change from baseline at Week 1 (n=203,201,201)	-1.0 (± 1.93)	-0.9 (± 2.22)	-0.9 (± 2.20)	
NS: Change from baseline at Week 2 (n=194,196,193)	-1.9 (± 2.72)	-1.9 (± 2.85)	-1.6 (± 2.64)	
NS: Change from baseline at Week 3 (n=188,186,185)	-2.2 (± 2.89)	-2.6 (± 3.26)	-2.1 (± 3.15)	
NS: Change from baseline at Week 4 (n=182,180,179)	-2.9 (± 3.17)	-3.5 (± 3.32)	-2.7 (± 3.51)	
NS: Change from baseline at Week 5 (n=174,178,174)	-3.2 (± 3.56)	-4.1 (± 3.83)	-2.9 (± 3.84)	
NS: Change from baseline at Week 6 (n=164,168,165)	-3.6 (± 3.91)	-4.2 (± 3.89)	-3.4 (± 4.02)	
GP: Change from baseline at Week 1 (n=203,201,201)	-3.0 (± 4.52)	-2.8 (± 4.30)	-2.4 (± 4.99)	
GP: Change from baseline at Week 2 (n=194,196,193)	-5.3 (± 5.80)	-5.7 (± 5.46)	-4.4 (± 5.68)	
GP: Change from baseline at Week 3 (n=188,186,185)	-6.8 (± 6.09)	-6.8 (± 6.01)	-5.8 (± 6.57)	
GP: Change from baseline at Week 4 (n=182,180,179)	-8.0 (± 6.53)	-9.2 (± 6.58)	-7.3 (± 7.30)	
GP: Change from baseline at Week 5 (n=174,178,174)	-9.1 (± 7.15)	-10.2 (± 6.95)	-8.1 (± 7.85)	
GP: Change from baseline at Week 6 (n=164,168,165)	-10.6 (± 7.49)	-11.5 (± 7.32)	-9.2 (± 7.59)	

Statistical analyses

Statistical analysis title	Treatment Comparison PANSS PS at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.273

Statistical analysis title	Treatment Comparison PANSS PS at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.274

Statistical analysis title	Treatment Comparison PANSS PS at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of

repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.062
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.364

Notes:

[37] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison PANSS PS at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	= 0.006
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	-0.29
Variability estimate	Standard error of the mean
Dispersion value	0.364

Notes:

[38] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison PANSS PS at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	= 0.012
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.416

Notes:

[39] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison PANSS PS at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[40]
P-value	= 0.004
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.417

Notes:

[40] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison PANSS PS at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	= 0.048
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.473

Notes:

[41] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison PANSS PS at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	-0.61
Variability estimate	Standard error of the mean
Dispersion value	0.474

Notes:

[42] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison PANSS PS at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[43]
P-value	= 0.002
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.58
upper limit	-0.56
Variability estimate	Standard error of the mean
Dispersion value	0.516

Notes:

[43] - Subjects in this analysis = 348.

Statistical analysis title	Treatment Comparison PANSS PS at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.06
upper limit	-1.03
Variability estimate	Standard error of the mean
Dispersion value	0.516

Notes:

[44] - Subjects in this analysis = 352.

Statistical analysis title	Treatment Comparison PANSS PS at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.03
upper limit	-0.86
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[45] - Subjects in this analysis = 329.

Statistical analysis title	Treatment Comparison PANSS PS at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.28
upper limit	-1.12
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[46] - Subjects in this analysis = 333.

Statistical analysis title	Treatment Comparison PANSS NS at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.316
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.205

Statistical analysis title	Treatment Comparison PANSS NS at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.653
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.204

Statistical analysis title	Treatment Comparison PANSS NS at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.12
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.266

Notes:

[47] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison PANSS NS at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[48]
P-value	= 0.232
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.265

Notes:

[48] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison PANSS NS at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	= 0.49
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.309

Notes:

[49] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison PANSS NS at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[50]
P-value	= 0.039
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.308

Notes:

[50] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison PANSS NS at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	= 0.173
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.331

Notes:

[51] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison PANSS NS at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[52]
P-value	= 0.005
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.331

Notes:

[52] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison PANSS NS at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[53]
P-value	= 0.137
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.378

Notes:

[53] - Subjects in this analysis = 348.

Statistical analysis title	Treatment Comparison PANSS NS at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[54]
P-value	= 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.98
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.377

Notes:

[54] - Subjects in this analysis = 352.

Statistical analysis title	Treatment Comparison PANSS NS at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[55]
P-value	= 0.181
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.405

Notes:

[55] - Subjects in this analysis = 329.

Statistical analysis title	Treatment Comparison PANSS NS at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[56]
P-value	= 0.01
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.404

Notes:

[56] - Subjects in this analysis = 333.

Statistical analysis title	Treatment Comparison PANSS GP at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.147
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.447

Statistical analysis title	Treatment Comparison PANSS GP at Week 1

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.502
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.448

Statistical analysis title	Treatment Comparison PANSS GP at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[57]
P-value	= 0.071
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.569

Notes:

[57] - Subjects in this analysis = 387.

Statistical analysis title	Treatment Comparison PANSS GP at Week 2

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[58]
P-value	= 0.028
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.37
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.569

Notes:

[58] - Subjects in this analysis = 389.

Statistical analysis title	Treatment Comparison PANSS GP at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	= 0.032
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.62
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.638

Notes:

[59] - Subjects in this analysis = 373.

Statistical analysis title	Treatment Comparison PANSS GP at Week 3

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[60]
P-value	= 0.062
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.638

Notes:

[60] - Subjects in this analysis = 371.

Statistical analysis title	Treatment Comparison PANSS GP at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[61]
P-value	= 0.058
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.73
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.708

Notes:

[61] - Subjects in this analysis = 361.

Statistical analysis title	Treatment Comparison PANSS GP at Week 4

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[62]
P-value	= 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.73
upper limit	-0.95
Variability estimate	Standard error of the mean
Dispersion value	0.708

Notes:

[62] - Subjects in this analysis = 359.

Statistical analysis title	Treatment Comparison PANSS GP at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[63]
P-value	= 0.031
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.22
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.781

Notes:

[63] - Subjects in this analysis = 348.

Statistical analysis title	Treatment Comparison PANSS GP at Week 5

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[64]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.19
upper limit	-1.12
Variability estimate	Standard error of the mean
Dispersion value	0.78

Notes:

[64] - Subjects in this analysis = 352.

Statistical analysis title	Treatment Comparison PANSS GP at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority[65]
P-value	= 0.006
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.91
upper limit	-0.65
Variability estimate	Standard error of the mean
Dispersion value	0.831

Notes:

[65] - Subjects in this analysis = 329.

Statistical analysis title	Treatment Comparison PANSS GP at Week 6

Statistical analysis description:

The mixed model for repeated measures includes treatment, country, visit, treatment by visit interaction, and baseline value as covariates, and participant as random effect. The correlation of repeated measures within a participant is estimated with an unstructured covariance matrix. The Kenward-Rogers method is used to estimate the denominator degrees of freedom.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	402
Analysis specification	Pre-specified
Analysis type	superiority[66]
P-value	< 0.001
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.79
upper limit	-1.54
Variability estimate	Standard error of the mean
Dispersion value	0.829

Notes:

[66] - Subjects in this analysis = 333.

Secondary: Percentage of PANSS Responders

End point title	Percentage of PANSS Responders

End point description:

The PANSS responders were defined as participants who have a >=30% reduction in PANSS total score between baseline and at each time point including Week 6. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score).

End point type	Secondary

End point timeframe:

Up to Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	203	
Units: Percentage of participants				
number (not applicable)				
At Week 1	2.5	1.5	2.5	
At Week 2	4.9	5.0	4.4	
At Week 3	10.3	10.4	7.9	
At Week 4	15.8	15.4	13.3	
At Week 5	22.2	25.4	17.2	
At Week 6	29.6	30.8	18.7	

Statistical analyses

Statistical analysis title	Treatment Comparison PANSS Responders at Week 1

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.993
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Treatment Comparison PANSS Responders at Week 1

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.481
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.173

Statistical analysis title	Treatment Comparison PANSS Responders at Week 2

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.784
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.117

Statistical analysis title	Treatment Comparison PANSS Responders at Week 2

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.837
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.117

Statistical analysis title	Treatment Comparison PANSS Responders at Week 3

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.375
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.086

Statistical analysis title	Treatment Comparison PANSS Responders at Week 3

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.381
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.086

Statistical analysis title	Treatment Comparison PANSS Responders at Week 4

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.419
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.071

Statistical analysis title	Treatment Comparison PANSS Responders at Week 4

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.554
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.072

Statistical analysis title	Treatment Comparison PANSS Responders at Week 5

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.162
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.063

Statistical analysis title	Treatment Comparison PANSS Responders at Week 5

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.061

Statistical analysis title	Treatment Comparison PANSS Responders at Week 6

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	High Dose Asenapine Maleate Transdermal Patch v Placebo
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.059

Statistical analysis title	Treatment Comparison PANSS Responders at Week 6

Statistical analysis description:

Estimates of the percentage of responders in each treatment group and differences of percentages between the treatment groups are based on the standard method based on the binomial distribution. 95% CIs for percentage estimates are based on the Wilson method. 95% CIs for the differences of percentage are based on the Newcombe method.

Comparison groups	Low Dose Asenapine Maleate Transdermal Patch v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference of Responders
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.058

Secondary: Change From Baseline in Calgary Depression Scale for Schizophrenia (CDSS) Score at Each Time Point

End point title	Change From Baseline in Calgary Depression Scale for Schizophrenia (CDSS) Score at Each Time Point

End point description:

The CDSS is a 9-item scale designed for assessment of level of depression in patients with schizophrenia. Each of 9 items was rated on a 4-point scale, scored from 0 to 3. The first 8 items were rated on basis of responses during a semistructured interview conducted by a qualified clinician. The ninth item (Observed Depression) was rated by evaluating signs and symptoms over course of interview. The total score was derived by adding each of 9 items together. Total scores of 6 or more identify presence of treatment emergent depression predictive of major depressive episodes. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0) through Week 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	201	201	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change from baseline at Week 1 (n=203, 201, 201)	-0.4 (± 1.82)	-0.4 (± 1.59)	-0.3 (± 1.58)	
Change from baseline at Week 2 (n=194, 196, 193)	-0.6 (± 1.87)	-0.7 (± 2.06)	-0.4 (± 1.99)	
Change from baseline at Week 3 (n=187, 186, 185)	-0.7 (± 2.03)	-0.7 (± 1.98)	-0.5 (± 1.97)	
Change from baseline at Week 4 (n=182, 180, 179)	-0.8 (± 2.05)	-1.0 (± 2.10)	-0.5 (± 2.36)	

Change from baseline at Week 5 (n=174, 178, 173)	-0.8 (± 1.99)	-0.9 (± 2.04)	-0.6 (± 2.14)	
Change from baseline at Week 6 (n=164, 168, 164)	-1.0 (± 1.93)	-1.0 (± 2.19)	-0.8 (± 1.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Medication Satisfaction Questionnaire (MSQ) Score at Each Time Point

End point title	Medication Satisfaction Questionnaire (MSQ) Score at Each Time Point

End point description:

The MSQ includes 1 simple question to ask patients about their satisfaction with their medication. A literature publication has evaluated of the psychometric properties in psychotic populations of the MSQ and found that responses to this 1 question were able to separate patients receiving active drug from those receiving placebo and was a good proxy for efficacy. As such, it was determined that a 1-point change on the MSQ may be considered clinically meaningful. Results were presented for participants in the FAS who had data available for analysis. The FAS included all randomized participants who had at least 1 patch of double-blind study medication applied and who have a baseline PANSS total score and at least 1 post baseline assessment of the primary efficacy measure (PANSS total score). Here, "n" denotes number of participants analysed at each specific time point.

End point type	Secondary

End point timeframe:

Week 2, 4 and 6

End point values	High Dose Asenapine Maleate Transdermal Patch	Low Dose Asenapine Maleate Transdermal Patch	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	199	194	192	
Units: Units on a scale				
arithmetic mean (standard deviation)				
At Week 2 (n=199, 194, 192)	4.7 (± 1.30)	4.7 (± 1.28)	4.5 (± 1.34)	
At Week 4 (n=184, 182, 181)	5.1 (± 1.16)	5.0 (± 1.28)	4.7 (± 1.47)	
At Week 6 (n=160, 169, 164)	5.2 (± 1.29)	5.3 (± 1.26)	4.9 (± 1.46)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose of doubleblind study medication (Day 1) through the 30 day follow-up period, approximately 72 days.

Adverse event reporting additional description:

The safety analysis set included all participants who had at least 1 patch of double-blind study medication applied and who have at least 1 post dose safety measurement during the double-blind treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	High Dose Asenapine Maleate Transdermal Patch

Reporting group description:

Participants in the high dose asenapine maleate transdermal patch treatment arm received 2 asenapine maleate transdermal patches, once daily for 42 days.

Reporting group title	Placebo

Reporting group description:

Participants in the Placebo arm received 2 placebo (matching with HP-3070) transdermal patches, once daily for 42 days.

Reporting group title	Low Dose Asenapine Maleate Transdermal Patch

Reporting group description:

Participants in the low dose asenapine maleate transdermal patch treatment arm received 1 asenapine maleate transdermal patch and 1 placebo (matching with HP-3070) transdermal patch, once daily for 42 days.

Serious adverse events	High Dose Asenapine Maleate Transdermal Patch	Placebo	Low Dose Asenapine Maleate Transdermal Patch
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 204 (0.98%)	4 / 206 (1.94%)	3 / 204 (1.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 204 (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
Overdose			

	High Dose Asenapine Maleate Transdermal Patch	Placebo	Low Dose Asenapine Maleate Transdermal Patch
subjects affected / exposed	0 / 204 (0.00%)	1 / 206 (0.49%)	0 / 204 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 204 (0.00%)	0 / 206 (0.00%)	1 / 204 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	0 / 206 (0.00%)	0 / 204 (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			
Schizophrenia			
subjects affected / exposed	1 / 204 (0.49%)	2 / 206 (0.97%)	2 / 204 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	High Dose Asenapine Maleate Transdermal Patch	Placebo	Low Dose Asenapine Maleate Transdermal Patch
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 204 (55.39%)	106 / 206 (51.46%)	110 / 204 (53.92%)
Investigations			
Weight increased			
subjects affected / exposed	12 / 204 (5.88%)	4 / 206 (1.94%)	8 / 204 (3.92%)
occurrences (all)	12	4	8
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 204 (9.31%)	13 / 206 (6.31%)	18 / 204 (8.82%)
occurrences (all)	21	13	23
Extrapyramidal disorder			
subjects affected / exposed	19 / 204 (9.31%)	3 / 206 (1.46%)	13 / 204 (6.37%)
occurrences (all)	22	4	16

General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	20 / 204 (9.80%)	3 / 206 (1.46%)	19 / 204 (9.31%)
occurrences (all)	57	14	105
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 204 (4.41%)	9 / 206 (4.37%)	11 / 204 (5.39%)
occurrences (all)	11	10	12
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 204 (6.86%)	23 / 206 (11.17%)	15 / 204 (7.35%)
occurrences (all)	16	28	21
Anxiety			
subjects affected / exposed	11 / 204 (5.39%)	13 / 206 (6.31%)	10 / 204 (4.90%)
occurrences (all)	13	19	14
Agitation			
subjects affected / exposed	6 / 204 (2.94%)	11 / 206 (5.34%)	5 / 204 (2.45%)
occurrences (all)	7	14	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2016	Removal of the proportion of CGI-I responders from the key secondary efficacy objectives and endpoints, and related statistical analysis sections. Addition of an irritation assessment at the site of patch application performed daily between 30 and 60 minutes after patch removal. Clarification to the potential advantages of HP 3070 over the current sublingual formulation of asenapine.
21 November 2016	Update of the exclusion criteria and key personnel. Clarification of the study procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported