Clinical trial results:
A Phase 2, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Efficacy, Safety, and Tolerability of Two Fixed Doses (15mg and 30 mg QD) of CVL-231 in Participants With Schizophrenia Experiencing an Acute Exacerbation of Psychosis

Summary

EudraCT number	2022-000581-17
Trial protocol	HU BG
Global end of trial date	11 September 2024
Results information	
Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification	
Sponsor protocol code	CVL-231-2002
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05227703
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 144,666

Notes:

Sponsors	
Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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	11 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 2 fixed oral doses (15 mg QD and 30 mg QD) of emraclidine in adult participants with schizophrenia experiencing an acute exacerbation of psychosis

Protection of trial subjects:

The investigator or his/her representative will explain the nature of the trial to the participant and answer all questions regarding the trial.
Participants must be informed that their participation is voluntary. Participants will be required to agree to (eg, provide electronic agreement or written signature) a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, privacy and data protection requirements, where applicable, and the IRB/IEC or trial center.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2022
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	Bulgaria: 29
Country: Number of subjects enrolled	Hungary: 14
Country: Number of subjects enrolled	United States: 348
Worldwide total number of subjects	391
EEA total number of subjects	43

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)	387

From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomly assigned at a ratio of 1:1:1 to one of three treatment groups (Emraclidine 15 mg QD, Emraclidine 30 mg QD, or Placebo). Randomization was stratified by geographic region (United States or all other countries). ITT population included all randomized participants and was used for the Demographic and Baseline Characteristics

Pre-assignment

Screening details:

The mITT population was used for the efficacy evaluations and included all randomized participants who received at least one dose of study drug, had a baseline assessment, and had at least 1 postbaseline PANSS assessment. FAS included all randomized participants who receive at least one dose of study drug and was used for the safety analysis.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a single daily oral dose of Placebo each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.

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

Dosage and administration details:

Matching placebo, oral (tablet), once per day for 6 weeks

Arm title	Emraclidine 15 mg QD

Arm description:

Participants received a single daily oral dose of Emraclidine 15 mg each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.

Arm type	Experimental
Investigational medicinal product name	Emraclidine 15 mg
Investigational medicinal product code	
Other name	CVL-231, ABBV-1231
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emraclidine 15 mg, oral (tablet), once per day for 6 weeks

Arm title	Emraclidine 30 mg QD

Arm description:

Participants received a single daily oral dose of Emraclidine 30 mg each morning from Day 1 (baseline)

through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.

Arm type	Experimental
Investigational medicinal product name	Emraclidine 30 mg
Investigational medicinal product code	
Other name	CVL-231, ABBV-1231
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emraclidine 30 mg, oral (tablet), once per day for 6 weeks

Number of subjects in period 1	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD
Started	130	130	131
Completed	102	93	93
Not completed	28	37	38
Physician decision	2	2	1
Consent withdrawn by subject	17	26	32
Adverse event, non-fatal	2	6	4
Not Specified	1	1	-
Non- Compliance with Study Schedule	-	1	-
Lack of efficacy	4	-	1
Protocol deviation	2	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a single daily oral dose of Placebo each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	
Reporting group title	Emraclidine 15 mg QD
Reporting group description:	
Participants received a single daily oral dose of Emraclidine 15 mg each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	
Reporting group title	Emraclidine 30 mg QD
Reporting group description:	
Participants received a single daily oral dose of Emraclidine 30 mg each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	

Reporting group values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD
Number of subjects	130	130	131
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42.1	42.7	41.5
standard deviation	± 12.18	± 11.51	± 10.76
Gender categorical Units: Subjects			
Female	27	34	25
Male	103	96	106
Ethnicity Units: Subjects			
Hispanic or Latino	30	25	25
Not Hispanic or Latino	100	105	106
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	76	83	85
White	53	44	44
More than one race	0	2	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	391		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	86		
Male	305		
Ethnicity Units: Subjects			
Hispanic or Latino	80		
Not Hispanic or Latino	311		
Unknown or Not Reported	0		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	2		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	244		
White	141		
More than one race	2		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a single daily oral dose of Placebo each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	
Reporting group title	Emraclidine 15 mg QD
Reporting group description:	
Participants received a single daily oral dose of Emraclidine 15 mg each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	
Reporting group title	Emraclidine 30 mg QD
Reporting group description:	
Participants received a single daily oral dose of Emraclidine 30 mg each morning from Day 1 (baseline) through Day 45. Participants (completers and early withdrawals) were followed for safety up to approximately 28 days after the last dose.	

Primary: Change From Baseline at Week 6 in the Positive and Negative Syndrome Scale (PANSS) Total Score

End point title	Change From Baseline at Week 6 in the Positive and Negative Syndrome Scale (PANSS) Total Score
End point description:	
The PANSS measures symptom severity of participants with schizophrenia and contains 7 positive symptom scales, 7 negative system scales, and 16 general psychopathology symptom scales. Participants are rated from 1 to 7 on each symptom scale with a total minimum score of 30 and a maximum score of 210. Baseline was defined as the last value obtained prior to initiation of investigational medicinal product (IMP). Change from baseline for a given endpoint was defined as the value on a given Study Day (Time Point) minus the Baseline Value. A decrease in PANSS total score correlates with an improvement in schizophrenia symptoms. Analysis population: Modified Intent-to-Treat population (mITT): All randomized participants who receive at least 1 dose of investigational medicinal product (IMP) and have both a baseline and at least 1 postbaseline PANSS assessment. Overall Number of Participants Analyzed includes participants with a non-missing value.	
End point type	Primary
End point timeframe:	
Baseline through Week 6	

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	94	96	
Units: score on a scale				
least squares mean (confidence interval 95%)	-16.1 (-19.4 to -12.8)	-18.5 (-22.0 to -15.0)	-14.2 (-17.5 to -10.8)	

Statistical analyses

Statistical analysis title	Placebo v Emraclidine 15mg QD

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Emraclidine 15 mg QD v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2925
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	2.3

Statistical analysis title	Placebo v Emraclidine 30mg QD

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3914
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	6.4
Variability estimate	Standard error of the mean
Dispersion value	2.27

Secondary: Change From Baseline at Week 6 in the Clinical Global Impression - Severity (CGI-S Score)

End point title	Change From Baseline at Week 6 in the Clinical Global

	Impression - Severity (CGI-S Score)

End point description:

The CGI-S captures clinician’s response to: "Considering your total clinical experience, how mentally ill is the participant at this time?" The clinician's answer rated on the following 7-point scale: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; 7 = among the most extremely ill participants. Baseline was defined as the last value obtained prior to initiation of investigational medicinal product (IMP). Change from baseline for a given endpoint was defined as the value on a given Study Day (Time Point) minus the Baseline Value. Negative changes from Baseline indicate less mental illness.

Analysis Population Description: mITT: All randomized participants who receive at least 1 dose of investigational medicinal product (IMP) and have both a baseline and at least 1 postbaseline PANSS assessment. Overall Number of Participants Analyzed includes participants with available data.

End point type	Secondary

End point timeframe:

Baseline through Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	94	96	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.83 (-1.03 to -0.64)	-1.05 (-1.25 to -0.84)	-0.80 (-1.00 to -0.60)	

Statistical analyses

Statistical analysis title	Placebo v Emraclidine 15 mg QD

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1165
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.135

Statistical analysis title	Placebo v Emraclidine 30 mg QD

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8265
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.134

Secondary: Change From Baseline at All Time Points in Positive and Negative Syndrome Scale (PANSS) Total Score

End point title	Change From Baseline at All Time Points in Positive and Negative Syndrome Scale (PANSS) Total Score

End point description:

The PANSS measures symptom severity of participants with schizophrenia and contains 7 positive symptom scales, 7 negative system scales, and 16 general psychopathology symptom scales. Participants are rated from 1 to 7 on each symptom scale with a total minimum score of 30 and a maximum score of 210. Baseline was defined as the last value obtained prior to initiation of investigational medicinal product (IMP). Change from baseline for a given endpoint was defined as the value on a given Study Day (Time Point) minus the Baseline Value. A decrease in PANSS total score correlates with an improvement in schizophrenia symptoms.
Analysis Population Description: mITT: All randomized participants who receive at least 1 dose of investigational medicinal product (IMP) and have both a baseline and at least 1 postbaseline PANSS assessment. Overall Number of Participants Analyzed includes participants with available data.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 3, 4, 5, and 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	122	123	
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 1 (n=128, 121, 123)	-5.0 (-6.9 to -3.1)	-6.8 (-8.8 to -4.8)	-4.9 (-6.8 to -2.9)	
Week 2 (n=122, 107, 118)	-8.5 (-10.9 to -6.1)	-8.7 (-11.2 to -6.3)	-7.5 (-9.9 to -5.1)	
Week 3 (n=119, 101, 116)	-11.2 (-13.8 to -8.5)	-12.5 (-15.3 to -9.7)	-10.0 (-12.6 to -7.3)	
Week 4 (n=114, 97, 101)	-12.8 (-15.5 to -10.1)	-13.4 (-16.3 to -10.5)	-12.0 (-14.8 to -9.2)	
Week 5 (n=109, 95, 98)	-14.7 (-17.7 to -11.6)	-16.5 (-19.7 to -13.2)	-12.9 (-16.0 to -9.8)	
Week 6 (n=104, 94, 96)	-16.1 (-19.4 to -12.8)	-18.5 (-22.0 to -15.0)	-14.2 (-17.5 to -10.8)	

Statistical analyses

Statistical analysis title	Week 1-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1167
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	1.14

Statistical analysis title	Week 1-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9254
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	1.14

Statistical analysis title	Week 2-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8792
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	2.8
Variability estimate	Standard error of the mean
Dispersion value	1.55

Statistical analysis title	Week 2-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5094
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4
Variability estimate	Standard error of the mean
Dispersion value	1.52

Statistical analysis title	Week 3-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4487
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	1.76

Statistical analysis title	Week 3-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4852
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	4.6
Variability estimate	Standard error of the mean
Dispersion value	1.72

Statistical analysis title	Week 4-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7593
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.1
Variability estimate	Standard error of the mean
Dispersion value	1.86

Statistical analysis title	Week 4-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6792
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	4.3
Variability estimate	Standard error of the mean
Dispersion value	1.82

Statistical analysis title	Week 5-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3983
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	2.1

Statistical analysis title	Week 5-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3859
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	5.9
Variability estimate	Standard error of the mean
Dispersion value	2.07

Statistical analysis title	Week 6-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2925
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	2.3

Statistical analysis title	Week 6-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3914
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	6.4
Variability estimate	Standard error of the mean
Dispersion value	2.27

Secondary: Change From Baseline at All Time Points in the Clinical Global Impression - Severity (CGI-S) Score

End point title	Change From Baseline at All Time Points in the Clinical Global Impression - Severity (CGI-S) Score

End point description:

The CGI-S captures clinician's response to: "Considering your total clinical experience, how mentally ill is the participant at this time?" The clinician's answer rated on the following 7-point scale: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; 7 = among the most extremely ill participants. Baseline was defined as the last value obtained prior to initiation of Emraclidine. Change from baseline for a given endpoint was defined as the value on a given Study Day (Time Point) minus the Baseline Value. Negative changes from Baseline indicate less mental illness.
Analysis Population Description: mITT: All randomized participants who receive at least 1 dose of investigational medicinal product (IMP) and have both a baseline and at least 1 postbaseline PANSS assessment. Overall Number of Participants Analyzed includes participants with available data.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 2, 3, 4, 5, and 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	122	123	
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 1 (n=128, 121, 122)	-0.21 (-0.33 to -0.09)	-0.33 (-0.46 to -0.21)	-0.21 (-0.33 to -0.09)	
Week 2 (n=122, 107, 118)	-0.42 (-0.56 to -0.28)	-0.42 (-0.56 to -0.27)	-0.38 (-0.52 to -0.24)	
Week 3 (n=119, 101, 116)	-0.55 (-0.70 to -0.40)	-0.64 (-0.80 to -0.48)	-0.49 (-0.64 to -0.34)	
Week 4 (n=114, 97, 101)	-0.72 (-0.88 to -0.55)	-0.74 (-0.91 to -0.57)	-0.62 (-0.79 to -0.46)	
Week 5 (n=109, 95, 98)	-0.78 (-0.96 to -0.60)	-0.91 (-1.10 to -0.72)	-0.69 (-0.87 to -0.51)	

Week 6 (n=104, 94, 96)	-0.83 (-1.03 to -0.64)	-1.05 (-1.25 to -0.084)	-0.80 (-1.00 to -0.60)	

Statistical analyses

Statistical analysis title	Week 1-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0865
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.073

Statistical analysis title	Week 1-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9921
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.14

Variability estimate	Standard error of the mean
Dispersion value	0.072

Statistical analysis title	Week 2-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.972
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.091

Statistical analysis title	Week 2-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6621
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.089

Statistical analysis title	Week 3-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3617
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.101

Statistical analysis title	Week 3-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5456
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.098

Statistical analysis title	Week 4-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3922
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.108

Statistical analysis title	Week 5-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2915
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.122

Statistical analysis title	Week 5-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit

interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Emraclidine 30 mg QD v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4425
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Week 4-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8459
Method	Mixed Model for Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Week 6-- Emraclidine 30 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8265
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.134

Statistical analysis title	Week 4-- Emraclidine 15 mg versus Placebo

Statistical analysis description:

Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8459
Method	Mixed Model for Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.11

Secondary: Percentage of Responders at Week 6 (Responders Defined as ≥30% Reduction From Baseline in PANSS Total Score)

End point title	Percentage of Responders at Week 6 (Responders Defined as ≥30% Reduction From Baseline in PANSS Total Score)

End point description:

The PANSS measures symptom severity of participants with schizophrenia and contains 7 positive symptom scales, 7 negative system scales, and 16 general psychopathology symptom scales. Participants are rated from 1 to 7 on each symptom scale with a total minimum score of 30 and a maximum score of 210. A PANSS responder is defined as a participant with at least a 30% change in PANSS total score compared to baseline at Week 6 or the early termination visit. If a subject discontinued and did not have an early termination visit, the subject's last assessment was considered. Analysis Population Description: mITT: All randomized participants who receive at least 1 dose of Emraclidine and have both a baseline and at least 1 postbaseline PANSS assessment. Overall Number of

Participants Analyzed includes participants with a non-missing value.

End point type	Secondary

End point timeframe:

Baseline through Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	122	123	
Units: percentage of participants				
number (not applicable)	19.5	23.8	12.2	

Statistical analyses

Statistical analysis title	Emraclidine 15 mg versus Placebo

Statistical analysis description:

Odds ratio, 95% confidence interval, and p-value were from a logistic regression with treatment group, geographic region and baseline value as a covariate.

Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4597
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.33

Statistical analysis title	Emraclidine 30 mg versus Placebo

Statistical analysis description:

Odds ratio, 95% confidence interval, and p-value were from a logistic regression with treatment group, geographic region and baseline value as a covariate.

Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1205
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.16

Secondary: Number of Participants With Treatment Emergent Adverse Event (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment Emergent Adverse Event (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment emergent adverse events/treatment-emergent serious adverse events (TEAEs/TESAEs) are defined as any event that
began or worsened in severity on or after the first dose of study drug.
Full analysis set: All randomized participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From first dose of study drug until 28 days following last dose of study drug (up to Week 10)

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants				
Any TEAE	69	65	65	
TESAE	1	3	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Electrocardiogram (ECGs)

End point title	Number of Participants With Clinically Significant Changes in Electrocardiogram (ECGs)

End point description:

Assessment of clinically significant changes in electrocardiogram measures measured by 12-lead ECG recording after the participant has been supine and at rest for at least 3 minutes.

Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP)

End point type	Secondary

End point timeframe:

Baseline; from first dose of study drug up to Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants				
QTcF value: > 450 - 480 msec	3	1	3	
QTcF value: > 480 - 500 msec	1	0	0	
QTcF value: > 500 msec	0	0	0	
QTcF increase from baseline: > 30 - 60 msec	7	10	10	
QTcF increase from baseline: > 60 msec	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Clinical Laboratory Assessments

End point title	Number of Participants With Clinically Significant Changes in Clinical Laboratory Assessments

End point description:

Clinical laboratory tests were performed at scheduled study visits, and the investigator recorded any clinically significant changes.

Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP)

End point type	Secondary

End point timeframe:

Baseline; from first dose of study drug up to Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants	3	4	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Vital Sign Measurements

End point title	Number of Participants With Clinically Significant Changes in Vital Sign Measurements

End point description:

Vital signs were obtained after the participant had been supine and at rest for 3 minutes and included temperature, systolic and diastolic blood pressure, respiratory rate, and heart rate. Participants' body weights were also measured and recorded.

Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP)

End point type	Secondary

End point timeframe:

Baseline; from first dose of study drug up to Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants				
Supine Systolic Blood Pressure (SBP): < 90 mmHg	0	0	0	
Supine SBP:> 140 mmHg and ≤ 160 mmHg	10	10	19	
Supine SBP:160 mmHg and ≤ 200 mmHg	0	0	0	
Supine SBP:> 200 mmHg	0	0	0	
Orthostatic Change in SBP:≥ 20 mmHg decrease	4	1	2	
Supine Diastolic Blood Pressure (DBP): < 50 mmHg	0	0	0	
Supine DBP:> 90 mmHg and ≤ 100 mmHg	5	12	19	
Supine DBP:> 100 mmHg and ≤ 120 mmHg	0	1	1	
Supine DBP: > 120 mmHg	0	0	0	
Orthostatic Change in DBP:≥ 10 mmHg decrease	3	12	5	
Supine Heart Rate: < 50 bpm	0	2	0	
Supine Heart Rate: ≥ 50 bpm and < 60 bpm	19	12	8	
Supine Heart Rate: > 100 bpm and ≤ 120 bpm	5	20	16	
Supine Heart Rate: > 120 bpm	0	0	1	
Temperature: < 36 °C	2	5	4	
Temperature: > 38 °C	2	0	0	
Respiratory Rate: < 12 breaths/min	0	1	0	
Respiratory Rate: > 20 breaths/min	3	1	3	
Weight: ≥ 7% decrease	6	0	4	
Weight: ≥ 7% increase	8	13	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Physical and Neurological Examination Results

End point title	Number of Participants With Clinically Significant Changes in Physical and Neurological Examination Results

End point description:

The number of participants with clinically significant changes in physical and neurological examination results was documented.

Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP)

End point type	Secondary

End point timeframe:

Baseline; from first dose of study drug up to Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants				
Clinically Significant Changes: Physical Exam	1	1	0	
Clinically Significant Changes: Neurological Exam	3	3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicide-Related Treatment-Emergent Events Assessed Using the Columbia Suicide- Severity Rating Scale (C-SSRS)

End point title	Number of Participants With Suicide-Related Treatment-Emergent Events Assessed Using the Columbia Suicide-Severity Rating Scale (C-SSRS)

End point description:

The C-SSRS rates an individual's degree of suicidal ideation (SI) on a scale, ranging from "wish to be dead" to "active suicidal ideation with specific plan and intent." The scale identifies SI severity and intensity, which may be indicative of an individual's intent to commit suicide. C-SSRS SI severity subscale ranges from 0 (no SI) to 5 (active SI with plan and intent).
Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP)

End point type	Secondary

End point timeframe:

Baseline; from first dose of study drug up to Week 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: Count of Participants				
Tx-Emergent Suicidal Ideation (Recently)	3	5	2	
Tx-Emergent Serious Suicidal Ideation (Recently)	0	0	0	
Emergence of Serious Suicidal Ideation (Recently)	0	0	0	
Emergence of Suicidal Behavior (Present vs Past)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simpson Angus Scale (SAS) Total Score

End point title	Change From Baseline in Simpson Angus Scale (SAS) Total Score

End point description:

The SAS consists of a list of 10 symptoms of parkinsonism. Each item is rated on a 5-point scale, with a score of 0 representing absence of symptoms and a score of 4 representing a severe condition. The SAS total score is the sum of the scores for all 10 items. Baseline was defined as the last value obtained prior to initiation of study drug. Change from baseline for a given endpoint was defined as the value on a given Study Day (Time Point) minus the Baseline Value. Negative changes from Baseline indicate an improvement in symptoms.

Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP); participants with available data.

End point type	Secondary

End point timeframe:

Baseline; Weeks 3 and 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 3 (n=123, 107, 119)	-0.1 (-0.1 to 0.0)	0.0 (-0.1 to 0.1)	0.0 (0.0 to 0.1)	
Week 6 (n=105, 92, 95)	0.0 (-0.1 to 0.1)	0.0 (0.0 to 0.1)	0.0 (-0.1 to 0.1)	

Statistical analyses

Statistical analysis title	Week 3-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0493
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[1] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 3-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0226
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[2] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.6845
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.06

Notes:

[3] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.895
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.06

Notes:

[4] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Secondary: Change From Baseline in Abnormal Involuntary Movement Scale (AIMS) Movement Rating Score

End point title	Change From Baseline in Abnormal Involuntary Movement Scale (AIMS) Movement Rating Score

End point description:

The AIMS assessment consists of 10 items describing symptoms of dyskinesia. Each item is rated on a 5-point scale, with a score of 0 representing absence of symptoms (for item 10, no awareness), and a score of 4 indicating a severe condition (for item 10, awareness, severe distress). In addition, the AIMS includes 2 yes/no questions that address the subject's dental status. Negative changes from Baseline indicate an improvement in symptoms.
Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP); participants with available data.

End point type	Secondary

End point timeframe:

Baseline; Weeks 3 and 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 3 (n=123, 107, 119)	0.0 (0.0 to 0.1)	0.0 (-0.1 to 0.1)	0.0 (-0.1 to 0.1)	
Week 6 (n=105, 92, 95)	0.0 (0.0 to 0.1)	0.0 (-0.1 to 0.0)	0.0 (0.0 to 0.1)	

Statistical analyses

Statistical analysis title	Week 3-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.5073
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[5] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 3-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.465
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[6] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.0672
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[7] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.803
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[8] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Secondary: Change From Baseline in Barnes Akathisia Rating Scale (BARS) Global Clinical Evaluation Score

End point title	Change From Baseline in Barnes Akathisia Rating Scale (BARS) Global Clinical Evaluation Score

End point description:

The BARS consists of 4 items related to akathisia: The first 3 items are rated on a 4-point scale, with a score of 0 representing absence of symptoms and a score of 3 representing a severe condition. The global clinical evaluation is made on a 6-point scale, with a score of 0 representing absence of symptom and a score of 5 representing severe akathisia. Negative changes from Baseline indicate an improvement in symptoms.
Analysis Population Description: Full analysis set: All randomized participants who received at least 1 dose of investigational medicinal product (IMP); participants with available data.

End point type	Secondary

End point timeframe:

Baseline; Weeks 3 and 6

End point values	Placebo	Emraclidine 15 mg QD	Emraclidine 30 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	130	131	
Units: score on a scale				
least squares mean (confidence interval 95%)				
Week 3 (n=123, 107, 119)	0.0 (-0.1 to 0.0)	0.0 (-0.1 to 0.0)	0.0 (-0.1 to 0.0)	
Week 6 (n=105, 92, 95)	-0.1 (-0.1 to 0.0)	0.0 (0.0 to 0.1)	0.0 (-0.1 to 0.0)	

Statistical analyses

Statistical analysis title	Week 3-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.8259
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[9] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 3-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD

Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.5936
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[10] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 15 mg versus Placebo
Comparison groups	Placebo v Emraclidine 15 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0253
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[11] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Statistical analysis title	Week 6-- Emraclidine 30 mg versus Placebo
Comparison groups	Placebo v Emraclidine 30 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.271
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[12] - Least-squares mean difference from Placebo and CIs were estimated using a mixed effects repeated measures model with fixed effects for treatment group, geographic region, visit, and treatment-by-visit interaction and Baseline value as a covariate. Participant was included as a random effect. An unstructured covariance structure was used.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse event tables include events reported from the time informed consent was signed to the end of the study. The median time on follow-up was 80, 67.5, and 64.0 days for Placebo, Emraclidine 15 mg, and Emraclidine 30 mg groups.

Adverse event reporting additional description:

respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Emraclidine_30_mg_QD
Reporting group description: -	
Reporting group title	Emraclidine_15_mg_QD
Reporting group description: -	

Serious adverse events	Placebo	Emraclidine_30_mg_QD	Emraclidine_15_mg_QD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 130 (0.77%)	1 / 131 (0.76%)	3 / 130 (2.31%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLEPTIC MALIGNANT SYNDROME			
subjects affected / exposed	1 / 130 (0.77%)	0 / 131 (0.00%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
VISION BLURRED			

subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
SCHIZOPHRENIA			
subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AGITATION			
subjects affected / exposed	0 / 130 (0.00%)	1 / 131 (0.76%)	0 / 130 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSYCHOTIC DISORDER			
subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE PSYCHOSIS			
subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	1 / 130 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Emraclidine_30_mg_QD	Emraclidine_15_mg_QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 130 (36.15%)	50 / 131 (38.17%)	47 / 130 (36.15%)
Investigations			
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 130 (0.00%)	1 / 131 (0.76%)	3 / 130 (2.31%)
occurrences (all)	0	1	3
WEIGHT INCREASED			
subjects affected / exposed	5 / 130 (3.85%)	4 / 131 (3.05%)	11 / 130 (8.46%)
occurrences (all)	5	4	11
Cardiac disorders			

SINUS TACHYCARDIA			
subjects affected / exposed	0 / 130 (0.00%)	0 / 131 (0.00%)	4 / 130 (3.08%)
occurrences (all)	0	0	5
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 130 (0.00%)	3 / 131 (2.29%)	2 / 130 (1.54%)
occurrences (all)	0	3	3
SOMNOLENCE			
subjects affected / exposed	6 / 130 (4.62%)	4 / 131 (3.05%)	4 / 130 (3.08%)
occurrences (all)	6	4	4
HEADACHE			
subjects affected / exposed	14 / 130 (10.77%)	17 / 131 (12.98%)	18 / 130 (13.85%)
occurrences (all)	17	19	19
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	3 / 130 (2.31%)	0 / 131 (0.00%)	4 / 130 (3.08%)
occurrences (all)	4	0	4
TOOTHACHE			
subjects affected / exposed	6 / 130 (4.62%)	2 / 131 (1.53%)	3 / 130 (2.31%)
occurrences (all)	6	2	3
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 130 (0.00%)	3 / 131 (2.29%)	1 / 130 (0.77%)
occurrences (all)	0	3	1
NAUSEA			
subjects affected / exposed	5 / 130 (3.85%)	4 / 131 (3.05%)	6 / 130 (4.62%)
occurrences (all)	5	4	6
CONSTIPATION			
subjects affected / exposed	2 / 130 (1.54%)	3 / 131 (2.29%)	6 / 130 (4.62%)
occurrences (all)	2	3	6
DRY MOUTH			
subjects affected / exposed	1 / 130 (0.77%)	7 / 131 (5.34%)	1 / 130 (0.77%)
occurrences (all)	1	7	1
DYSPEPSIA			
subjects affected / exposed	2 / 130 (1.54%)	3 / 131 (2.29%)	4 / 130 (3.08%)
occurrences (all)	2	3	4
Psychiatric disorders			

ANXIETY			
subjects affected / exposed	4 / 130 (3.08%)	4 / 131 (3.05%)	4 / 130 (3.08%)
occurrences (all)	4	4	4
INSOMNIA			
subjects affected / exposed	4 / 130 (3.08%)	4 / 131 (3.05%)	2 / 130 (1.54%)
occurrences (all)	4	4	2
SUICIDAL IDEATION			
subjects affected / exposed	3 / 130 (2.31%)	3 / 131 (2.29%)	0 / 130 (0.00%)
occurrences (all)	3	3	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	3 / 130 (2.31%)	3 / 131 (2.29%)	0 / 130 (0.00%)
occurrences (all)	3	3	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 130 (0.00%)	1 / 131 (0.76%)	3 / 130 (2.31%)
occurrences (all)	0	1	3
Infections and infestations			
TINEA PEDIS			
subjects affected / exposed	0 / 130 (0.00%)	3 / 131 (2.29%)	0 / 130 (0.00%)
occurrences (all)	0	3	0
TOOTH ABSCESS			
subjects affected / exposed	2 / 130 (1.54%)	3 / 131 (2.29%)	0 / 130 (0.00%)
occurrences (all)	2	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2022	Key changes in Protocol CVL-231-2002 Version 2.0 include: updating the drug name to its International Nonproprietary Name (emraclidine); adding a EudraCT number for EU compliance; updating sponsor and signatory information; expanding the upper age limit from 55 to 65 to broaden eligibility; clarifying participant stratification by region; allowing flexibility in medical monitor contact and urine drug screen procedures; and providing more detail on statistical analyses (MMRM and sensitivity analyses). Laboratory protocols were revised for SARS-CoV-2 testing and vital signs now require triplicate measurement in line with AHA standards. Dietary restrictions were clarified to prohibit grapefruit or Seville orange products. The document also refined criteria for inclusion/exclusion (e.g., contraception for men, language modernization of disability terms, stricter antihypertensive therapy requirements, and higher threshold for exclusionary heart rate). Prohibitions on medications prolonging QT interval were lifted due to emraclidine’s profile. Other changes address biospecimen collection, nonclinical paragraph removal, language improvements for clarity, alignment with regulatory guidance (CTFG, DSM-5), and enhanced sections on liver test assessment and sample collection. Overall, these amendments aim to improve protocol clarity, increase trial inclusiveness, meet regulatory requirements, and ensure participant safety.
15 March 2023	Key changes in Protocol CVL-231-2002 Version 3.0 include changes and updates focusing on clarifying trial procedures. The Signature Page was updated to reflect new sponsor signatories due to changes in internal responsibilities. In the Synopsis, references to extending enrollment because of COVID-19 impacts were removed, and statistical methods were revised for clearer handling of intercurrent events. The Schedule of Assessments saw clarifications in PK sampling footnotes to aid site procedures. Exclusion Criteria were adjusted, relaxing COVID-19 testing requirements to allow site-specific procedures. The exclusion of participants with a positive hepatitis B core antibody was removed, now focusing on active hepatitis B risk. Participants from previous trials without treatment for a year can now enroll, pending medical monitor approval. For Prohibited Therapy, the washout period for specific antipsychotic agents was reduced to align with other trials for acute schizophrenia. Adverse event instructions were enhanced with guidance for grading blood pressure-related events. Clinical Laboratory Tests now allow SARS-CoV-2 tests at the investigator's discretion. The follow-up period for pregnant participants was specified not to exceed 12 weeks post-estimated delivery, aligning with guidelines for pregnant partners of male participants. The Cytochrome P450 3A Inducers/Inhibitors table was updated to reflect current medication standards. Generally, minor grammatical and wording corrections were made for clarity. Overall, the amendment streamlines processes, incorporates updated guidance, and enhances the clarity of trial procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported