Clinical trial results:
A Phase 2B Randomized, Double-Blind, Placebo- and Active-Controlled Trial of the Efficacy and Safety of MK-8189 in Participants Experiencing an Acute Episode of Schizophrenia

Summary

EudraCT number	2020-000094-24
Trial protocol	LV PL BG HR
Global end of trial date	21 June 2024

Results information

Result version number	v1
This version publication date	06 July 2025
First version publication date	06 July 2025

Trial information

Trial identification

Sponsor protocol code	MK-8189-008

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2024
Global end of trial reached?	Yes
Global end of trial date	21 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of MK-8189 at a range of doses (8 mg, 16 mg, and 24 mg once daily [QD]) in adult participants who have an acute episode of schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders 5thEdition (DSM-5) criteria. The primary hypotheses were the following: (1)that MK-8189 24 mg is superior to placebo in reducing the Week 6 mean change from baseline in Positive and Negative Syndrome Scale (PANSS)total score, and (2) that MK-8189 16 mg is superior to placebo in reducing the Week 6 mean change from baseline in PANSS total score. With Amendment 4, enrollment was changed to approximately 500 participants with removal of the MK-8189 8 mg treatment arm. Participants enrolled before Amendment 4 who were assigned to MK-8189 8 mg QD remained on that dose regimen per protocol.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 47
Country: Number of subjects enrolled	Croatia: 29
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Romania: 18
Country: Number of subjects enrolled	Russian Federation: 25
Country: Number of subjects enrolled	Serbia: 32
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Ukraine: 28
Country: Number of subjects enrolled	United States: 294
Worldwide total number of subjects	499
EEA total number of subjects	109

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)	499
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled and randomized at 75 study sites in 11 countries.

Pre-assignment

Screening details:

Randomization into the MK-8189 8 mg arm ceased as of Amendment 4.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-8189 8 mg

Arm description:

Participants received MK-8189 8 mg once daily (QD) from Weeks 1 to 12, with 2 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	MK-8189
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-8189 administered QD at a dose of 8 mg,16 mg, or 24 mg via oral tablet.

Arm title	MK-8189 16 mg

Arm description:

Participants received MK-8189 16 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	MK-8189
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-8189 administered QD at a dose of 8 mg,16 mg, or 24 mg via oral tablet.

Arm title	MK-8189 24 mg

Arm description:

Participants received MK-8189 24 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.

Arm type	Experimental
Investigational medicinal product name	MK-8189
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-8189 administered QD at a dose of 8 mg,16 mg, or 24 mg via oral tablet.

Arm title	Risperidone 6 mg

Arm description:

Participants received risperidone 6 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.

Arm type	Active comparator
Investigational medicinal product name	Risperidone
Investigational medicinal product code	
Other name	RISPERDAL
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Risperidone administered QD at a dose of 6 mg via oral capsule.

Arm title	Placebo and MK-8189 24 mg

Arm description:

Participants received placebo QD from Weeks 1 to 6 and MK-8189 24 mg from Weeks 7 to 12, with 2 weeks of follow-up.

Arm type	Placebo
Investigational medicinal product name	MK-8189
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MK-8189 administered QD at a dose of 8 mg,16 mg, or 24 mg via oral tablet.

Number of subjects in period 1	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg
Started	41	132	132
Completed	14	64	61
Not completed	27	68	71
Adverse event, serious fatal	-	1	-
Physician decision	3	8	15
Consent withdrawn by subject	19	44	40
Miscellaneous	3	12	9
Lost to follow-up	2	3	7

Number of subjects in period 1	Risperidone 6 mg	Placebo and MK-8189 24 mg
Started	65	129
Completed	37	70
Not completed	28	59
Adverse event, serious fatal	-	-

Physician decision	2	11
Consent withdrawn by subject	21	39
Miscellaneous	4	6
Lost to follow-up	1	3

Baseline characteristics

Reporting groups	
Reporting group title	MK-8189 8 mg
Reporting group description:	
Participants received MK-8189 8 mg once daily (QD) from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	MK-8189 16 mg
Reporting group description:	
Participants received MK-8189 16 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	MK-8189 24 mg
Reporting group description:	
Participants received MK-8189 24 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	Risperidone 6 mg
Reporting group description:	
Participants received risperidone 6 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	Placebo and MK-8189 24 mg
Reporting group description:	
Participants received placebo QD from Weeks 1 to 6 and MK-8189 24 mg from Weeks 7 to 12, with 2 weeks of follow-up.	

Reporting group values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg
Number of subjects	41	132	132
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)	41	132	132
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	35.7	39.4	36.9
standard deviation	± 8.9	± 9.0	± 9.2
Sex: Female, Male Units:			
Female	12	46	42
Male	29	86	90
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	3	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	18	59	59

White	20	68	70
More than one race	1	1	1
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	14	10
Not Hispanic or Latino	40	117	121
Unknown or Not Reported	0	1	1

Reporting group values	Risperidone 6 mg	Placebo and MK-8189 24 mg	Total
Number of subjects	65	129	499
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)	65	129	499
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	38.5	40.2	
standard deviation	± 9.6	± 9.2	-
Sex: Female, Male Units:			
Female	25	42	167
Male	40	87	332
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	4	12
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	29	57	222
White	34	66	258
More than one race	1	2	6
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	11	40
Not Hispanic or Latino	61	118	457
Unknown or Not Reported	0	0	2

End points

End points reporting groups

Reporting group title	MK-8189 8 mg
Reporting group description:	
Participants received MK-8189 8 mg once daily (QD) from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	MK-8189 16 mg
Reporting group description:	
Participants received MK-8189 16 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	MK-8189 24 mg
Reporting group description:	
Participants received MK-8189 24 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	Risperidone 6 mg
Reporting group description:	
Participants received risperidone 6 mg QD from Weeks 1 to 12, with 2 weeks of follow-up.	
Reporting group title	Placebo and MK-8189 24 mg
Reporting group description:	
Participants received placebo QD from Weeks 1 to 6 and MK-8189 24 mg from Weeks 7 to 12, with 2 weeks of follow-up.	

Primary: Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 6

End point title	Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 6

End point description:

The PANSS assesses the severity of schizophrenia symptoms through a 30-item clinician-rated inventory organized into a positive subscale (7 items), a negative subscale (7 items) and a general psychopathology subscale (16 items). For each item, symptoms are rated on a 7-point scale from 1 (absent) to 7 (extreme). The PANSS total score for each participant was calculated as the sum of the rating assigned to each of the 30 PANSS items, and ranges from 30 (lowest total score) to 210 (highest total score). Higher and lower change scores reflect symptom worsening and improvement, respectively. Per protocol, the effect of the 8 mg dose was not assessed; risperidone and placebo were active and inactive controls, respectively. All participants who receive ≥1 dose of MK-8189 (16 mg or 24 mg), risperidone, or placebo, and have both a baseline measurement and ≥1valid post-baseline assessment, are included.

End point type	Primary

End point timeframe:

Baseline and Week 6

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	85	68	42
Units: Score on a scale				
least squares mean (confidence interval 95%)	(to)	-20.7 (-24.1 to -17.3)	-18.5 (-22.1 to -15.0)	-24.0 (-28.8 to -19.2)

Notes:

[1] - Per protocol, the MK-8189 8 mg arm was excluded from the analysis.

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Score on a scale				
least squares mean (confidence interval 95%)	-17.8 (-21.2 to -14.5)			

Statistical analyses

Statistical analysis title	MK-8189 24 mg PANSS Week 6
Comparison groups	MK-8189 24 mg v Placebo and MK-8189 24 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.784
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-6.3
upper limit	4.9

Statistical analysis title	MK-8189 16 mg PANSS Week 6
Comparison groups	MK-8189 16 mg v Placebo and MK-8189 24 mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.241
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-8.3
upper limit	2.6

Primary: Number of participants who experience one or more adverse events (AEs)

End point title	Number of participants who experience one or more adverse events (AEs)[2]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporarily associated with the use of study intervention, whether or not considered related to the study intervention. Per protocol, events were assessed for the first 6 weeks of treatment. All participants who received ≥1 dose of study intervention are included.

End point type	Primary

End point timeframe:

Up to Week 6

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	132	132	65
Units: Participants	29	85	94	31

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Participants	70			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who discontinued from study intervention due to AE

End point title	Number of participants who discontinued from study intervention due to AE[3]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporarily associated with the use of study intervention, whether or not considered related to the study intervention. Per protocol, events were assessed for the first 6 weeks of treatment. All participants who received ≥1 dose of study intervention are included.

End point type	Primary

End point timeframe:

Up to Week 6

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	132	132	65
Units: Participants	8	17	33	8

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Participants	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in PANSS positive subscale (PSS) score at Week 6

End point title	Change from baseline in PANSS positive subscale (PSS) score at Week 6

End point description:

The PANSS Positive Subscale (PSS) assesses the severity of schizophrenia symptoms. The PANSS PSS score was calculated as the sum of the rating assigned to each of the 7 PSS items and ranges from 7 (lowest total score) to 49 (highest total score). Higher and lower change scores reflect symptom worsening and improvement, respectively. Per protocol, the effect of the 8 mg dose was not assessed; risperidone and placebo were active and inactive controls, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[4]	85	68	42
Units: Score on a scale				
least squares mean (confidence interval 95%)	(to)	-7.1 (-8.2 to -6.0)	-7.2 (-8.3 to -6.0)	-7.7 (-9.3 to -6.1)

Notes:

[4] - Per protocol, the MK-8189 8 mg arm was excluded from the analysis.

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Score on a scale				
least squares mean (confidence interval	-5.8 (-6.9 to			

95%)	-4.7)

Statistical analyses

Statistical analysis title	MK-8189 24 mg PANSS PSS Week 6
Comparison groups	MK-8189 24 mg v Placebo and MK-8189 24 mg
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.094
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.2
upper limit	0.5

Statistical analysis title	MK-8189 16 mg PANSS PSS Week 6
Comparison groups	MK-8189 16 mg v Placebo and MK-8189 24 mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.096
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.1
upper limit	0.5

Secondary: Change from baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Week 6

End point title	Change from baseline in Clinical Global Impression-Severity of Illness (CGI-S) score at Week 6

End point description:

The CGI-S is a single item 7-point clinician rated scale for assessing the global severity of the participant’s illness. CGI-S scores range from 1 (participant normal, not ill) to 7 (participant extremely ill); higher and lower change from baseline scores indicate symptom worsening and improvement, respectively. Per protocol, the effect of the 8 mg dose was not assessed; risperidone and placebo were active and inactive controls, respectively.

End point type	Secondary
End point timeframe:	
Baseline and Week 6	

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	83	68	42
Units: Score on a scale				
least squares mean (confidence interval 95%)	(to)	-1.1 (-1.3 to -0.9)	-1.0 (-1.2 to -0.8)	-1.3 (-1.5 to -1.0)

Notes:

[5] - Per protocol, the MK-8189 8 mg arm was excluded from the analysis.

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: Score on a scale				
least squares mean (confidence interval 95%)	-1.0 (-1.2 to -0.8)			

Statistical analyses

Statistical analysis title	MK-8189 24 mg CGI-S Week 6
Comparison groups	MK-8189 24 mg v Placebo and MK-8189 24 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.959
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.3
upper limit	0.3

Statistical analysis title	MK-8189 16 mg CGI-S Week 6
Comparison groups	MK-8189 16 mg v Placebo and MK-8189 24 mg

Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.254
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.5
upper limit	0.1

Secondary: Change from baseline in body weight at Week 12

End point title	Change from baseline in body weight at Week 12

End point description:

The change from baseline in body weigh was determined at Week 12. Negative and positive values represent body weight loss and gain from baseline, respectively. Weight was measured using a standardized scale. Per protocol, the effect of the 8 mg dose was not assessed; risperidone and placebo were active and inactive controls, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[6]	56	45	34
Units: Kilograms				
least squares mean (confidence interval 95%)	(to)	-5.4 (-6.5 to -4.4)	-4.3 (-5.4 to -3.2)	3.0 (1.6 to 4.4)

Notes:

[6] - Per protocol, the MK-8189 8 mg arm was excluded from the analysis.

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Kilograms				
least squares mean (confidence interval 95%)	-2.3 (-3.4 to -1.3)			

Statistical analyses

Statistical analysis title	MK-8189 24 mg Body Weight Week 12
Comparison groups	MK-8189 24 mg v Risperidone 6 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-7.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-9.3
upper limit	-5.2

Statistical analysis title	MK-8189 16 mg Body Weight Week 12
Comparison groups	MK-8189 16 mg v Risperidone 6 mg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-8.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-10.4
upper limit	-6.5

Secondary: Change from baseline in body weight at Week 6

End point title	Change from baseline in body weight at Week 6

End point description:

The change from baseline in body weigh was determined at Week 6. Negative and positive values represent body weight loss and gain from baseline, respectively. Weight was measured using a standardized scale. Per protocol, the effect of the 8 mg dose was not assessed; risperidone and placebo were active and inactive controls, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	MK-8189 8 mg	MK-8189 16 mg	MK-8189 24 mg	Risperidone 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	86	75	44
Units: Kilograms				
least squares mean (confidence interval 95%)	(to)	-3.2 (-3.9 to -2.5)	-2.8 (-3.5 to -2.1)	2.8 (1.8 to 3.8)

Notes:

[7] - Per protocol, the MK-8189 8 mg arm was excluded from the analysis.

End point values	Placebo and MK-8189 24 mg			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Kilograms				
least squares mean (confidence interval 95%)	0.5 (-0.2 to 1.2)			

Statistical analyses

Statistical analysis title	MK-8189 24 mg Body Weight Week 6
Comparison groups	MK-8189 24 mg v Risperidone 6 mg
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.4
upper limit	-2.1

Statistical analysis title	MK-8189 16 mg Body Weight Week 6
Comparison groups	MK-8189 16 mg v Risperidone 6 mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.7

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.8
upper limit	-2.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~14 weeks

Adverse event reporting additional description:

All treated participants are included. To accommodate the different treatments in the "Placebo and MK-8189 24 mg", data from Weeks 1 to 6 and Weeks 7 to 12 are presented separately.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	MK-8189 8 mg Weeks 1 to 6

Reporting group description:

Participants received MK-8189 8 mg QD from Weeks 1 to 6.

Reporting group title	MK-8189 16 mg Weeks 1 to 6

Reporting group description:

Participants (who received MK-8189 16 mg Weeks 1 to 6) received MK-8189 16 mg QD from Weeks 1 to 6.

Reporting group title	MK-8189 24 mg Weeks 1 to 6

Reporting group description:

Participants received MK-8189 24 mg QD from Weeks 1 to 6.

Reporting group title	Risperidone 6 mg Weeks 1 to 6

Reporting group description:

Participants received risperidone 6 mg QD from Weeks 1 to 6.

Reporting group title	Placebo Weeks 1 to 6

Reporting group description:

Participants received placebo QD from Weeks 1 to 6.

Reporting group title	MK-8189 16 mg Weeks 7 to 12

Reporting group description:

Participants (who received MK-8189 16 mg Weeks 1 to 6) received MK-8189 16 mg QD from Weeks 7 to 12.

Reporting group title	MK-8189 8 mg Weeks 7 to 12

Reporting group description:

Participants (who received MK-8189 8 mg Weeks 1 to 6) received MK-8189 8 mg QD from Weeks 7 to 12.

Reporting group title	Risperidone 6 mg Weeks 7 to 12

Reporting group description:

Participants (who received risperidone 6 mg Weeks 1 to 6) received risperidone 8 mg QD from Weeks 7 to 12.

Reporting group title	MK-8189 24 mg Weeks 7 to 12

Reporting group description:

Participants (who received MK-8189 24 mg) received MK-8189 24 mg QD from Weeks 7 to 12.

Reporting group title	MK-8189 24 mg Weeks 7 to 12 (Placebo Weeks 1 to 6)

Reporting group description:

Participants (who received placebo Weeks 1 to 6) received MK-8189 24 mg Weeks 7 to 12.

Serious adverse events	MK-8189 8 mg Weeks 1 to 6	MK-8189 16 mg Weeks 1 to 6	MK-8189 24 mg Weeks 1 to 6
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 41 (2.44%)	8 / 132 (6.06%)	6 / 132 (4.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Completed suicide			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 132 (1.52%)	5 / 132 (3.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle rigidity			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (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
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Risperidone 6 mg Weeks 1 to 6	Placebo Weeks 1 to 6	MK-8189 16 mg Weeks 7 to 12
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 65 (3.08%)	0 / 129 (0.00%)	4 / 75 (5.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 65 (1.54%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	1 / 65 (1.54%)	0 / 129 (0.00%)	3 / 75 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle rigidity			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			

subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MK-8189 8 mg Weeks 7 to 12	Risperidone 6 mg Weeks 7 to 12	MK-8189 24 mg Weeks 7 to 12
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	0 / 39 (0.00%)	3 / 60 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 39 (0.00%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Muscle rigidity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MK-8189 24 mg Weeks 7 to 12 (Placebo Weeks 1 to 6)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 85 (2.35%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Subarachnoid haemorrhage			

subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			

subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle rigidity			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MK-8189 8 mg Weeks 1 to 6	MK-8189 16 mg Weeks 1 to 6	MK-8189 24 mg Weeks 1 to 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 41 (43.90%)	58 / 132 (43.94%)	72 / 132 (54.55%)
Investigations			
Weight increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Akathisia			
subjects affected / exposed	0 / 41 (0.00%)	8 / 132 (6.06%)	12 / 132 (9.09%)
occurrences (all)	0	9	12
Dystonia			
subjects affected / exposed	2 / 41 (4.88%)	4 / 132 (3.03%)	9 / 132 (6.82%)
occurrences (all)	2	4	10
Headache			
subjects affected / exposed	4 / 41 (9.76%)	12 / 132 (9.09%)	11 / 132 (8.33%)
occurrences (all)	4	12	13
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 41 (2.44%)	7 / 132 (5.30%)	3 / 132 (2.27%)
occurrences (all)	1	7	4
Diarrhoea			
subjects affected / exposed	3 / 41 (7.32%)	6 / 132 (4.55%)	3 / 132 (2.27%)
occurrences (all)	3	6	3
Nausea			
subjects affected / exposed	2 / 41 (4.88%)	21 / 132 (15.91%)	25 / 132 (18.94%)
occurrences (all)	2	25	30
Toothache			
subjects affected / exposed	3 / 41 (7.32%)	1 / 132 (0.76%)	0 / 132 (0.00%)
occurrences (all)	3	1	0
Vomiting			
subjects affected / exposed	4 / 41 (9.76%)	16 / 132 (12.12%)	18 / 132 (13.64%)
occurrences (all)	4	21	34
Reproductive system and breast disorders			
Erectile dysfunction			

subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 41 (9.76%)	7 / 132 (5.30%)	10 / 132 (7.58%)
occurrences (all)	4	11	13
Anxiety			
subjects affected / exposed	2 / 41 (4.88%)	8 / 132 (6.06%)	13 / 132 (9.85%)
occurrences (all)	2	8	13
Agitation			
subjects affected / exposed	4 / 41 (9.76%)	7 / 132 (5.30%)	3 / 132 (2.27%)
occurrences (all)	5	8	3
Schizophrenia			
subjects affected / exposed	2 / 41 (4.88%)	6 / 132 (4.55%)	11 / 132 (8.33%)
occurrences (all)	2	6	11
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 132 (2.27%)	3 / 132 (2.27%)
occurrences (all)	0	3	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 132 (0.00%)	0 / 132 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Risperidone 6 mg Weeks 1 to 6	Placebo Weeks 1 to 6	MK-8189 16 mg Weeks 7 to 12
Total subjects affected by non-serious adverse events			

subjects affected / exposed	19 / 65 (29.23%)	45 / 129 (34.88%)	18 / 75 (24.00%)
Investigations			
Weight increased			
subjects affected / exposed	3 / 65 (4.62%)	3 / 129 (2.33%)	0 / 75 (0.00%)
occurrences (all)	3	3	0
Nervous system disorders			
Akathisia			
subjects affected / exposed	4 / 65 (6.15%)	2 / 129 (1.55%)	1 / 75 (1.33%)
occurrences (all)	4	2	1
Dystonia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 65 (6.15%)	12 / 129 (9.30%)	2 / 75 (2.67%)
occurrences (all)	4	12	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 65 (1.54%)	5 / 129 (3.88%)	2 / 75 (2.67%)
occurrences (all)	1	6	4
Diarrhoea			
subjects affected / exposed	0 / 65 (0.00%)	5 / 129 (3.88%)	1 / 75 (1.33%)
occurrences (all)	0	5	3
Nausea			
subjects affected / exposed	6 / 65 (9.23%)	6 / 129 (4.65%)	3 / 75 (4.00%)
occurrences (all)	11	7	6
Toothache			
subjects affected / exposed	2 / 65 (3.08%)	1 / 129 (0.78%)	1 / 75 (1.33%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	1 / 65 (1.54%)	7 / 129 (5.43%)	4 / 75 (5.33%)
occurrences (all)	4	8	5
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 65 (0.00%)	1 / 129 (0.78%)	1 / 75 (1.33%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	1 / 65 (1.54%)	1 / 129 (0.78%)	0 / 75 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 65 (1.54%)	8 / 129 (6.20%)	7 / 75 (9.33%)
occurrences (all)	1	8	7
Anxiety			
subjects affected / exposed	4 / 65 (6.15%)	8 / 129 (6.20%)	2 / 75 (2.67%)
occurrences (all)	4	12	3
Agitation			
subjects affected / exposed	1 / 65 (1.54%)	2 / 129 (1.55%)	0 / 75 (0.00%)
occurrences (all)	1	2	0
Schizophrenia			
subjects affected / exposed	2 / 65 (3.08%)	7 / 129 (5.43%)	1 / 75 (1.33%)
occurrences (all)	2	7	1
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 65 (1.54%)	3 / 129 (2.33%)	1 / 75 (1.33%)
occurrences (all)	1	3	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 129 (0.00%)	1 / 75 (1.33%)
occurrences (all)	0	0	1

Non-serious adverse events	MK-8189 8 mg Weeks 7 to 12	Risperidone 6 mg Weeks 7 to 12	MK-8189 24 mg Weeks 7 to 12
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 17 (23.53%)	9 / 39 (23.08%)	10 / 60 (16.67%)
Investigations			
Weight increased			

subjects affected / exposed	0 / 17 (0.00%)	2 / 39 (5.13%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Akathisia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Dystonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 17 (0.00%)	2 / 39 (5.13%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 39 (2.56%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 39 (2.56%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	0	3
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1

Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	2 / 60 (3.33%)
occurrences (all)	0	0	2
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	1 / 39 (2.56%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Agitation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Schizophrenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 39 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 39 (0.00%)	0 / 60 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	2 / 39 (5.13%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	2 / 39 (5.13%)	1 / 60 (1.67%)
occurrences (all)	0	2	1

Non-serious adverse events	MK-8189 24 mg Weeks 7 to 12 (Placebo Weeks 1 to 6)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 85 (29.41%)		
Investigations			
Weight increased			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
Nervous system disorders			

Akathisia			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	4		
Dystonia			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	4		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	5 / 85 (5.88%)		
occurrences (all)	5		
Toothache			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			

subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	4		
Anxiety			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	5		
Agitation			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	2		
Schizophrenia			
subjects affected / exposed	6 / 85 (7.06%)		
occurrences (all)	6		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Nephrolithiasis			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2020	AM1: The primary purpose was to update the number of capsules for risperidone due to change in dose.
24 November 2020	AM2: The primary purpose was to update exclusion criterion per FDA feedback.
17 December 2021	AM3: The primary purpose was to increase flexibility in eligibility criteria due to enrollment challenges.
16 November 2022	AM4: The primary purpose was to end enrollment into the MK-8189 8 mg arm.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported