Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy, safety, tolerability, and pharmacokinetics of single subcutaneous MIJ821 injection in addition to standard of care in participants with treatment-resistant depression

Summary

EudraCT number	2021-005992-38
Trial protocol	ES PL
Global end of trial date	28 November 2023

Results information

Result version number	v2 (current)
This version publication date	13 June 2025
First version publication date	12 December 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CMIJ821B12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05454410
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	28 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of MIJ821 (versus placebo) in treatment resistant depression (TRD) after single subcutaneous (s.c.) injection.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Rescue medications were allowed and the use of these were documented in the medical records and in the electronic case report form (eCRF). Prohibited medication was administered as rescue medication if clinically warranted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 2023
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	Japan: 3
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	60
EEA total number of subjects	44

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All inclusion and exclusion criteria were checked during screening and on Day 1, prior to randomization.

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	MIJ821 10 mg

Arm description:

Participants received a single dose of 10 mg MIJ821 administered as a subcutaneous (SC) injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	MIJ821
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single dose of 10 mg MIJ821 administered as a subcutaneous (SC) injection on Day 1.

Arm title	MIJ821 4 mg

Arm description:

Participants received a single dose of 4 mg MIJ821 administered as a SC injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	MIJ821
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single dose of 4 mg MIJ821 administered as a SC injection on Day 1.

Arm title	MIJ821 1 mg

Arm description:

Participants received a single dose of 1 mg MIJ821 administered as a SC injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	MIJ821
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single dose of 1 mg MIJ821 administered as a SC injection on Day 1.

Arm title	Placebo

Arm description:

Participants received a single dose of 0.9% sodium chloride solution administered as a SC injection on Day 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single dose of 0.9% sodium chloride solution administered as a SC injection on Day 1.

Number of subjects in period 1	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg
Started	15	14	14
Completed	15	14	13
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	Placebo
Started	17
Completed	16
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	MIJ821 10 mg
Reporting group description:	
Participants received a single dose of 10 mg MIJ821 administered as a subcutaneous (SC) injection on Day 1.	
Reporting group title	MIJ821 4 mg
Reporting group description:	
Participants received a single dose of 4 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	MIJ821 1 mg
Reporting group description:	
Participants received a single dose of 1 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single dose of 0.9% sodium chloride solution administered as a SC injection on Day 1.	

Reporting group values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg
Number of subjects	15	14	14
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)	15	14	14
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	47.8	43.9	46.9
standard deviation	± 12.36	± 11.29	± 9.73
Sex/Gender, Customized Units: participants			
Male	4	4	5
Female	11	10	9
Race/Ethnicity, Customized Units: Subjects			
White	15	13	12
American Indian or Alaska Native	0	0	0
Asian / Japanese	0	1	2
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	2	3	3
Not Hispanic or Latino	13	11	11
Unknown or Not Reported	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	17	60	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	17	60	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	47.1		
standard deviation	± 12.05	-	
Sex/Gender, Customized Units: participants			
Male	10	23	
Female	7	37	
Race/Ethnicity, Customized Units: Subjects			
White	17	57	
American Indian or Alaska Native	0	0	
Asian / Japanese	0	3	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	8	
Not Hispanic or Latino	17	52	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	MIJ821 10 mg
Reporting group description:	
Participants received a single dose of 10 mg MIJ821 administered as a subcutaneous (SC) injection on Day 1.	
Reporting group title	MIJ821 4 mg
Reporting group description:	
Participants received a single dose of 4 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	MIJ821 1 mg
Reporting group description:	
Participants received a single dose of 1 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single dose of 0.9% sodium chloride solution administered as a SC injection on Day 1.	
Subject analysis set title	Overall
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pooled for all participants	

Primary: Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score 24 Hours (Day 2) after Injection

End point title	Change from Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score 24 Hours (Day 2) after Injection
End point description:	
The Montgomery Åsberg Depression Rating Scale (MADRS, SIGMA version), is a clinician rated scale designed to measure depression severity and detects changes due to antidepressant treatment. The test consists of 10 items, each of which is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 0 - 60. Higher scores represent a more severe condition. The MADRS evaluates apparent sadness, reported sadness, inner tension, sleep, appetite, concentration, lassitude, interest level, pessimistic thoughts and suicidal thoughts. The MADRS scores were collected electronically by qualified personnel.	
End point type	Primary
End point timeframe:	
Baseline and 24 hours after SC injection	

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	17
Units: Scores on a Scale				
least squares mean (standard error)	-14.1 (± 1.95)	-11.4 (± 2.04)	-8.4 (± 2.02)	-8.9 (± 1.82)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	MIJ821 10 mg v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-5.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.6
upper limit	-0.7

Statistical analysis title	Statistical Analysis 2
Comparison groups	MIJ821 4 mg v Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-2.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7
upper limit	2.1

Statistical analysis title	Statistical Analysis 3
Comparison groups	MIJ821 1 mg v Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4
upper limit	5.1

Secondary: Percentage of Participants with Treatment-Emergent Adverse Events

(TEAEs), including Adverse Events of Special Interest (AESIs)

End point title	Percentage of Participants with Treatment-Emergent Adverse Events (TEAEs), including Adverse Events of Special Interest (AESIs)

End point description:

A TEAE was defined as an adverse event starting or worsening after the administration of study medication and up to the end of study visit. The following events were considered AESIs:

- Dissociation
- Sedation
- Cardiovascular effects (Blood Pressure changes and QT interval prolongation on electrocardiogram [ECG])
- Respiratory effects (difficulty in breathing, changes in oxygen saturation)
- Suicidality (suicidal ideation or behavior)
- Memory gaps/amnesia
- Cystitis or lower urinary tract adverse events

End point type	Secondary

End point timeframe:

From Day 1 after SC injection to end of study, up to 29 Days

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	17
Units: Percentage of participants				
number (not applicable)				
With at least one AE	66.67	42.86	28.57	41.18
With at least one AESI	60	35.71	14.29	17.65
Blood pressure increased	0	7.14	7.14	0
Dissociation	33.33	14.29	0	11.76
Derealization	6.67	0	0	0
Vision blurred	0	0	7.14	0
Amnesia	6.67	0	0	0
Somnolence	26.67	7.14	0	5.88
Sedation	6.67	7.14	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of MIJ821 in Plasma for Area Under the Curve from the Time of Dosing to the Time of the Last Measurable Concentration (AUClast)

End point title	Pharmacokinetics (PK) of MIJ821 in Plasma for Area Under the Curve from the Time of Dosing to the Time of the Last Measurable Concentration (AUClast)[1]

End point description:

Blood samples were collected at the indicated time points for PK analysis. AUClast was defined as the area under the curve from time zero to the last measurable concentration sampling time (tlast).

End point type	Secondary

End point timeframe:

Baseline, 0.17 hour, 0.33 hour, 0.5 hour, 0.75 hour, 1, 1.5, 2, 4 and 24 hours post injection

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only analyzed in the MIJ821 arms.

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	13	
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	231 (± 33.5)	89.5 (± 45.7)	5.92 (± 85.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK of MIJ821 in Plasma for Maximum Serum Concentration (Cmax)

End point title	PK of MIJ821 in Plasma for Maximum Serum Concentration (Cmax)[2]

End point description:

Blood samples were collected at the indicated time points for PK analysis. Cmax was defined as the maximum (peak) observed plasma drug concentration after single dose administration.

End point type	Secondary

End point timeframe:

Baseline, 0.17 hour, 0.33 hour, 0.5 hour, 0.75 hour, 1, 1.5, 2, 4 and 24 hours post injection

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only analyzed in the MIJ821 arms.

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	13	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	42.7 (± 37.2)	17.5 (± 46.7)	2.32 (± 55.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK of MIJ821 in Plasma for Time to Maximum Drug Concentration (Tmax)

End point title	PK of MIJ821 in Plasma for Time to Maximum Drug Concentration (Tmax)[3]

End point description:

Blood samples were collected at the indicated time points for PK analysis. Tmax was defined as the time to reach maximum (peak) plasma drug concentration after single dose administration (time).

End point type	Secondary

End point timeframe:

Baseline, 0.17 hour, 0.33 hour, 0.5 hour, 0.75 hour, 1, 1.5, 2, 4 and 24 hours post injection

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only analyzed in the MIJ821 arms.

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	14	
Units: hour (h)				
median (full range (min-max))	0.750 (0.333 to 2.00)	0.500 (0.150 to 1.00)	0.500 (0.167 to 0.783)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the MADRS Total Scores at Day 8, 15, 22 and 29 Visits

End point title	Change from Baseline in the MADRS Total Scores at Day 8, 15, 22 and 29 Visits

End point description:

The MADRS (SIGMA version), is a clinician rated scale designed to measure depression severity and detects changes due to antidepressant treatment. The test consists of 10 items, each of which is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 0 - 60. Higher scores represent a more severe condition. The MADRS evaluates apparent sadness, reported sadness, inner tension, sleep, appetite, concentration, lassitude, interest level, pessimistic thoughts and suicidal thoughts. The MADRS scores were collected electronically by qualified personnel.

End point type	Secondary

End point timeframe:

Baseline, Days 8, 15, 22 and 29

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	17
Units: Scores on a Scale				
least squares mean (standard error)				
Change from Baseline (Day 8) n=15,14,14,17	-15.3 (± 2.0)	-9.9 (± 2.1)	-8.2 (± 2.0)	-7.4 (± 1.8)
Change from Baseline (Day 15) n=14,13,14,17	-14.0 (± 2.2)	-8.5 (± 2.2)	-11.0 (± 2.2)	-7.7 (± 2.0)
Change from Baseline (Day 22) n=14,14,13,17	-14.9 (± 2.2)	-10.7 (± 2.3)	-9.7 (± 2.3)	-7.0 (± 2.0)
Change from Baseline (Day 29) n=14,14,13,16	-14.9 (± 2.3)	-12.7 (± 2.4)	-10.7 (± 2.4)	-7.0 (± 2.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Dose-response (DR) Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score at 24 Hours after Single SC injection

End point title	Dose-response (DR) Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score at 24 Hours after Single SC injection

End point description:

The multiple comparison procedure - modelling (MCP-Mod) approach was an integrated approach used to investigate DR relationships, while confirming efficacy of the test product based on hypothesis testing. A set of candidate models was tested using Multiple Comparison Procedures (MCP) that preserve the family-wise error rate (FWER) to determine the model best representing the underlying DR. Efficacy via DR was established when at least one of the model tests was significant.

End point type	Secondary

End point timeframe:

Baseline up to 24 Hours

End point values	MIJ821 10 mg	MIJ821 4 mg	MIJ821 1 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	17
Units: Scores on a Scale				
least squares mean (standard error)	-14.1 (± 1.95)	-11.4 (± 2.04)	-8.4 (± 2.02)	-8.9 (± 1.82)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MCP-Mod was used to check if there was a DR relationship between the change from baseline to 24 hours in MADRS total score and the doses received. The Least squares means under the primary estimand were used to test the null hypothesis of a flat DR relationship at a one-sided significance level of 5% against the alternative hypothesis of a non-flat DR curve. Six candidate DR curves were used to derive the optimal model contrasts for the multiple contrast tests. A monotone DR was assumed.

Comparison groups	MIJ821 10 mg v MIJ821 4 mg v MIJ821 1 mg v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0242 [4]
Method	Multiple contrast test

Notes:

[4] - P-value for the selected model best representing the underlying DR (the lowest p-value out of the 6 candidate models), adjusted for multiple comparisons.

Secondary: Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameters: placebo effect E0, Emax

End point title	Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameters: placebo effect E0, Emax

End point description:

The exposure-response (ER) relationship was investigated considering PK exposure parameters (AUClast and Cmax) and the change from baseline MADRS score derived at 4 h and 24 h after injection and Day 8, Day 15, Day 22 and Day 29 during the follow-up. The emax model or sigmoid emax model were planned to be fitted for the change from baseline at each follow up visit and the PK exposure parameters, Cmax and AUClast. If the model converges, parameters estimated from the Sigmoid emax model are: the placebo effect E0, EC50, Emax and the hill parameter.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 15, 22 and 29

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: Scores on a scale				
number (not applicable)				
ER Relationship Cmax: placebo effect E0	999			
ER Relationship Cmax: Emax	999			
ER Relationship AUClast: placebo effect E0	999			
ER Relationship AUClast: Emax	999			

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameter: EC50 (AUClast)

End point title	Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameter: EC50 (AUClast)

End point description:

The exposure-response (ER) relationship was investigated considering PK exposure parameters (AUClast and Cmax) and the change from baseline MADRS score derived at 4 h and 24 h after injection and Day 8, Day 15, Day 22 and Day 29 during the follow-up. The emax model or sigmoid emax model were planned to be fitted for the change from baseline at each follow up visit and the PK exposure parameters, Cmax and AUClast. If the model converges, parameters estimated from the Sigmoid emax model are: the placebo effect E0, EC50, Emax and the hill parameter.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 15, 22 and 29

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: h*ng/mL				
number (not applicable)				
ER Relationship AUClast: EC50	999			

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameter: EC50 (Cmax)

End point title	Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameter: EC50 (Cmax)

End point description:

The exposure-response (ER) relationship was investigated considering PK exposure parameters (AUClast and Cmax) and the change from baseline MADRS score derived at 4 h and 24 h after injection and Day 8, Day 15, Day 22 and Day 29 during the follow-up. The emax model or sigmoid emax model were planned to be fitted for the change from baseline at each follow up visit and the PK exposure parameters, Cmax and AUClast. If the model converges, parameters estimated from the Sigmoid emax model are: the placebo effect E0, EC50, Emax and the hill parameter.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 15, 22 and 29

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: ng/mL				
number (not applicable)				
ER Relationship Cmax: EC50	999			

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated parameter: Hill Parameter

End point title	Exposure-response Relationship of MIJ821 with Respect to Change from Baseline in MADRS Total Score. Estimated

	parameter: Hill Parameter

End point description:

The exposure-response (ER) relationship was investigated considering PK exposure parameters (AUClast and Cmax) and the change from baseline MADRS score derived at 4 h and 24 h after injection and Day 8, Day 15, Day 22 and Day 29 during the follow-up. The emax model or sigmoid emax model were planned to be fitted for the change from baseline at each follow up visit and the PK exposure parameters, Cmax and AUClast. If the model converges, parameters estimated from the Sigmoid emax model are: the placebo effect E0, EC50, Emax and the hill parameter.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 15, 22 and 29

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: Hill coefficient				
number (not applicable)				
ER Relationship Cmax: Hill parameter	999			
ER Relationship AUClast: Hill parameter	999			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from first dose of study treatment until end of study treatment, up to a maximum duration of 29 days.	
Adverse event reporting additional description:	
The Safety Analysis Set included all participants who received any study drug. Participants were analyzed according to the study treatment received.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	MIJ821 10mg
Reporting group description:	
Participants received a single dose of 10 mg MIJ821 administered as a subcutaneous (SC) injection on Day 1.	
Reporting group title	MIJ821 4mg
Reporting group description:	
Participants received a single dose of 4 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	MIJ821 1mg
Reporting group description:	
Participants received a single dose of 1 mg MIJ821 administered as a SC injection on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single dose of 0.9% sodium chloride solution administered as a SC injection on Day 1.	
Reporting group title	All MIJ821
Reporting group description:	
All MIJ821 Dosages	
Reporting group title	All Subjects
Reporting group description:	
All Subjects included in the Safety Analysis Set	

Serious adverse events	MIJ821 10mg	MIJ821 4mg	MIJ821 1mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo	All MIJ821	All Subjects
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 43 (0.00%)	0 / 60 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	MIJ821 10mg	MIJ821 4mg	MIJ821 1mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 15 (66.67%)	6 / 14 (42.86%)	4 / 14 (28.57%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Heart rate increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Somnolence			
subjects affected / exposed	4 / 15 (26.67%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	4	1	0
Sedation			
subjects affected / exposed	1 / 15 (6.67%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Amnesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Tension headache			

subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Dissociation			
subjects affected / exposed	5 / 15 (33.33%)	2 / 14 (14.29%)	0 / 14 (0.00%)
occurrences (all)	5	2	0
Derealisation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Depression			

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo	All MIJ821	All Subjects
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 17 (41.18%)	20 / 43 (46.51%)	27 / 60 (45.00%)
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 17 (0.00%)	2 / 43 (4.65%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Heart rate increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 17 (5.88%)	5 / 43 (11.63%)	6 / 60 (10.00%)
occurrences (all)	1	5	6

Sedation			
subjects affected / exposed	0 / 17 (0.00%)	2 / 43 (4.65%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Headache			
subjects affected / exposed	3 / 17 (17.65%)	4 / 43 (9.30%)	7 / 60 (11.67%)
occurrences (all)	4	4	8
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	1 / 43 (2.33%)	2 / 60 (3.33%)
occurrences (all)	1	1	2
Amnesia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Tension headache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 17 (0.00%)	3 / 43 (6.98%)	3 / 60 (5.00%)
occurrences (all)	0	3	3
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	2 / 17 (11.76%)	0 / 43 (0.00%)	2 / 60 (3.33%)
occurrences (all)	2	0	2
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			

subjects affected / exposed	1 / 17 (5.88%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Psychiatric disorders			
Dissociation			
subjects affected / exposed	2 / 17 (11.76%)	7 / 43 (16.28%)	9 / 60 (15.00%)
occurrences (all)	2	7	9
Derealisation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Tooth infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 43 (2.33%)	1 / 60 (1.67%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2022	Amendment 01 includes the following: The purpose of this protocol amendment was to clarify that the End of-Study visit (Day 29) was the last study visit for ensuring safety follow-up and thus a safety follow-up call at Day 31 was not required while taking into consideration the pharmacokinetic profile of MIJ821 (five times the apparent terminal elimination half-life of MIJ821). The protocol was amended to clarify that in case of extended safety monitoring for adverse events on Day 1, between 4 hours and 24 hours post-dose, additional safety tests or measures were required, including but not limited to, unscheduled PK samples. The recall periods for the MADRS and the Clinical Global Impression - Severity (CGI-S) scale were added in order to adequately assess efficacy at the 4 hour-time point on Day 1. In addition, the recall period of the MADRS used at screening had specified: “Last 7 days with euthymic baseline”. The recall period of the Clinician-Administered Dissociative States Scale (CADSS) was also added. The recall period of the Columbia-Suicide Severity Rating Scale (C-SSRS) at the first study visit was updated to reflect that this version assessed suicidal ideation and suicidal behavior during the participant's last one year and during a predefined period of one month.
04 November 2022	Amendment 02 includes the following: The purpose of this protocol amendment was to replace the Mini International Neuropsychiatric Interview (M.I.N.I), used at screening to assess whether the diagnostic criteria was met, with an equivalent validated instrument: the Structured Clinical Interview for DSM-5 Disorders (SCID-5). The M.I.N.I was not to be used in this trial due to difficulties related to copyright license agreement's activities, which were not to be overcome in a timely manner.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: