NOVARTIS

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

MIJ821

Trial Indication(s)

Major Depressive Disorder

Protocol Number

CMIJ821A12201

Protocol Title

A double-blind, placebo-controlled, randomized dose-ranging trial to investigate efficacy and safety of intravenous MIJ821 infusion in addition to comprehensive standard of care on the rapid reduction of symptoms of Major Depressive Disorder in subjects who have suicidal ideation with intent

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II:

NOVARTIS

Study Start/End Dates

Study Start Date: July 20, 2021 (Actual)
Primary Completion Date: September 26, 2023 (Actual)
Study Completion Date: September 26, 2023 (Actual)

Reason for Termination (If applicable)

Terminated by Novartis

Study Design/Methodology

This was a Phase 2b double-blind, placebo-controlled, randomized, parallel-group dose-ranging study to investigate the efficacy and safety of 4 doses of intravenous MIJ821 administered on Day 1, 15 and 29 as a 40-min infusion in addition to comprehensive SoC for the rapid reduction of the symptoms of MDD in participants who have suicidal ideation with intent. Comprehensive SoC included initial hospitalization and pharmacological antidepressant therapy (antidepressant monotherapy or an antidepressant plus augmentation). In addition, the study explored the effect for single dose administration of 0.16 mg/kg and 0.048 mg/kg given once on Day 1 to treat MDD in participants who have suicidal ideation with intent.

Centers

39 centers in 14 countries: United States(6), Spain(6), Turkey(3), Malaysia(2), Poland(5), Russia(2), Netherlands(1), Japan(3), Mexico(3), Germany(2), Taiwan(2), Brazil(2), Canada(1), Argentina(1)

Objectives:

Primary objective: The primary objective of this study was to investigate the dose response relationship for 4 doses (0.0048, 0.016, 0.048 and 0.16 mg/kg) of MIJ821 vs. placebo arm. The primary clinical question of interest was: what is the effect of MIJ821 versus placebo in conjunction with pharmacological standard of care (SoC) on change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) total score at 24 hours post first dose administration, in participants

with Major Depressive Disorder (MDD) who have suicidal ideation with intent, accounting for intercurrent events (IEs) with potential confounding effects and IEs leading to study discontinuation prior to the 24 hours assessment.

Secondary objective: In terms of efficacy, the secondary objectives assessed the effect of MIJ821 on the proportion of participants meeting MADRS response and remission criteria over time during the Core Period and after first infusion in the Extension Period and examined sustained MADRS response and remission criteria. Other secondary objectives were to assess MIJ821 pharmacokinetics in plasma and to assess safety and tolerability of MIJ821.

Test Product (s), Dose(s), and Mode(s) of Administration

During the Core period, in all treatment arms, investigational treatment was administered by intravenous infusion every other week, 3 infusions in total. During the Extension period if relapse criteria were met, participants were treated with the same blinded MIJ821 dose and regimen they received during the Core period, receiving three i.v. infusions of investigational treatment once every 2 weeks, for a total period of 6 weeks, and participants treated with placebo in Core period were rerandomized to one of the MIJ821 treatments.

Statistical Methods

Primary endpoint: The primary endpoint is the change in MADRS total score from Baseline (Day 1, predose) to 24 hours post first dose in the Core Period. The adjusted mean (and standard error) of primary endpoint at each individual dose were obtained from analysis of covariance (ANCOVA) model including region, treatment as factors and baseline MADRS as covariate.

Secondary endpoints: For response rate and remission rate, sustained response rate and remission rate, the frequency summary (count and proportion) were provided for those endpoints by analysis visit.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Signed informed consent must be obtained prior to participation in the study

2. Male and female participants, 18 to 65 years of age (inclusive) at screening

3. DSM-5 defined major depressive disorder (MDD) with a current major depressive episode (MDE) without psychotic features at the time of screening based upon clinical assessment and confirmed by the Mini International Neuropsychiatric Interview (M.I.N.I.) assessed at Screening

4. Participants must have current suicidal ideation with intent, confirmed by a "Yes" response to Question B3 AND either Question B10 or Question B11 obtained from the M.I.N.I., assessed at Screening

5. Current suicidal ideation with intent, confirmed by "Yes" response to Question 3 AND either Question 9 or Question 10 obtained from the SSTS at Baseline

6. Montgomery-Åsberg Depression Rating Scale (MADRS) score > 28 at Screening and before randomization on Day 1

7. Participants must agree to receive pharmacological standard of care treatment to treat their MDD (as determined by the treating physician(s) based on clinical judgement and local treatment guidelines) during the trial duration

8. In the physician's opinion, acute psychiatric hospitalization is clinically warranted to treat the patient’s condition, and the patient is either already in the hospital or agrees to be hospitalized voluntarily for the required per protocol period

Exclusion Criteria:

1. Any prior or current diagnosis of bipolar disorder, MDD with psychotic features, schizophrenia, or schizoaffective disorder as obtained from M.I.N.I. at Screening

2. Patients with acute alcohol or substance use disorder or withdrawal symptoms requiring detoxification, or patients who went through detoxification treatment (inpatient or outpatient) within 1 month before Screening.

3. Participant has a current clinical diagnosis of autism, dementia, or intellectual disability

4. History of seizures. Note: childhood febrile seizures are not exclusionary

5. Participants with current borderline personality disorder as obtained from M.I.N.I. at Screening.

6. Participants with suicidal ideation or behavior caused primarily by another non-MDD condition as obtained from M.I.N.I. at Screening

7. Participants taking medications prohibited by the protocol

8. Intake of the following medications/ psychotherapy:

a. Esketamine or Ketamine 2 months before Screening
b. Current Monoamine oxidase inhibitors (MAOIs) 14 days before Screening

c. known worsening or new appearance of suicidal ideation or behavior during a prior treatment, or within 2 months after last administration

9. Any other condition (e.g. known liver disease/liver dysfunction, active malignancy, etc.) which in the opinion of the investigator would put the safety of the participant at risk, impede compliance or hinder completion of the study.

Participant Flow Table

Core Period: 6 weeks

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo	Total
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29	
Started	30	32	25	18	32	28	34	199
Full Analysis and Safety Set	29	32	25	18	32	28	33	197
Completed	25	29	23	15	28	26	30	176
Not Completed	5	3	2	3	4	2	4	23

Withdrawal by Subject	3	2	1	2	4	1	1	14
Physician Decision	2	0	0	1	0	0	2	5
Lost to Follow-up	0	1	0	0	0	1	0	2
progressive disease	0	0	1	0	0	0	0	1
Death	0	0	0	0	0	0	1	1

Extension Period

	MIJ821 0.16 mg/kg bi-weekly	**MIJ821 0.048 mg/kg bi-weekly**	**MIJ821 0.016 mg/kg bi-weekly**	**MIJ821 0.0048 mg/kg bi-weekly**	**MIJ821 0.16 mg/kg single dose**	**MIJ821 0.048 mg/kg single dose**	**Placebo**	**Total**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29	
Started	23	26	22	14	25	25	28	163
52 Weeks Extension	16	18	17	9	16	16	22	114
8 Weeks Follow-Up	7	8	5	5	9	9	6	49
Completed	11	10	11	8	12	14	11	77
Not Completed	12	16	11	6	13	11	17	86

Study terminated by sponsor	7	8	4	5	9	7	8	48
Withdrawal by Subject	3	5	1	1	2	2	4	18
Progressive disease	1	1	3	0	0	1	1	7
Lost to Follow-up	0	1	2	0	1	0	1	5
Physician Decision	0	0	1	0	1	0	1	3
Guardian decision	1	0	0	0	0	0	0	1
New therapy for study indication	0	0	0	0	0	0	1	1
Pregnancy	0	0	0	0	0	1	0	1
Protocol Violation	0	0	0	0	0	0	1	1
Unsatisfactory therapeutic effect	0	1	0	0	0	0	0	1

Baseline Characteristics

	MIJ821 0.16 mg/kg bi-weekly	**MIJ821 0.048 mg/kg bi-weekly**	**MIJ821 0.016 mg/kg bi-weekly**	**MIJ821 0.0048 mg/kg bi-weekly**	**MIJ821 0.16 mg/kg single dose**	**MIJ821 0.048 mg/kg single dose**	**Placebo**	**Total**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40	MIJ821 0.048 mg/kg dose for 40	MIJ821 0.016 mg/kg dose for 40	MIJ821 0.0048 mg/kg dose	MIJ821 0.16 mg/kg dose for 40	MIJ821 0.048 mg/kg dose for 40	40 minutes IV infusion of 0.9% sodium	

	minutes on Day 1, Day 15 and Day 29	minutes IV infusion on Day 1, Day 15 and Day 29	minutes IV infusion on Day 1, Day 15 and Day 29	for 40 minutes IV infusion on Day 1, Day 15 and Day 29	minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	chloride on Day 1, Day 15 and Day 29	
Number of Participants [units: participants]	30	32	25	18	32	28	34	199
Baseline Analysis Population Description								
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation								
	38.3±14.24	39.2±12.11	37.7±9.63	30.6±9.21	43.2±13.11	41.6±15.30	37.5±15.42	38.8±13.43
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
Female	16	16	12	13	18	19	15	109
Male	14	16	13	5	14	9	19	90
Race (NIH/OMB) (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
American Indian or Alaska Native	0	1	0	0	0	0	0	1
Asian	5	4	3	6	2	5	2	27
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0
Black or African American	1	1	0	0	0	2	5	9

White	24	26	22	12	30	21	27	162
More than one race	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0

Primary Outcome Result(s)

Change from baseline in the total score of the Montgomery Åsberg Depression Rating Scale (MADRS)

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 was collected electronically by qualified personnel. Since the MADRS total score at 24 hours was evaluated post the single first infusion (prior to the second infusion), the bi-weekly and single dosing regimens of the same dose level are pooled as one arm for 0.048 mg/kg and 0.16 mg/kg.
Time Frame	Baseline, 24 hours
Analysis Population Description	Full Analysis Set (all randomized and treated participants)

	MIJ821 0.16 mg/kg	**MIJ821 0.048 mg/kg**	**MIJ821 0.016 mg/kg**	**MIJ821 0.0048 mg/kg**	**Placebo**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion	40 minutes IV infusion of 0.9% sodium chloride
Number of Participants Analyzed [units: participants]	61	60	25	18	33
Change from baseline in the total score of the Montgomery Åsberg Depression Rating Scale (MADRS) (units: unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**

-16.4 ± 1.18	-17.2 ± 1.19	-17.7 ± 1.84	-12.7 ± 2.19	-17.5 ± 1.60

Secondary Outcome Result(s)

Number of participants with treatment-emergent adverse events (TEAEs) and adverse events of special interest (AESI) during the core period

Description	Treatment-emergent adverse events (TEAEs) and adverse events of special interest (AESIs) in Core period
Time Frame	6 weeks
Analysis Population Description	Safety Set

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Number of Participants Analyzed [units: participants]	29	32	25	18	32	28	33
Number of participants with treatment-emergent	**Count of Participants**	**Count of Participants**	**Count of Participants**	**Count of Participants**	**Count of Participants**	**Count of Participants**	**Count of Participants**

adverse events (TEAEs) and adverse events of special interest (AESI) during the core period (units: participants)	**(Not Applicable)**	**(Not Applicable)**	**(Not Applicable)**	**(Not Applicable)**	**(Not Applicable)**	**(Not Applicable)**	**(Not Applicable)**
Number of participants with at least one TEAE	19 (65.52%)	24 (75%)	15 (60%)	14 (77.78%)	16 (50%)	23 (82.14%)	16 (48.48%)
Number of participants with TEAEs leading to study treatment discontinuation	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Number of participants with at least one Treatment-emergent serious adverse events (TESAEs)	1 (3.45%)	0 (%)	2 (8%)	3 (16.67%)	0 (%)	1 (3.57%)	3 (9.09%)
Number of participants with any adverse event of special interest (AESIs)	15 (51.72%)	8 (25%)	9 (36%)	7 (38.89%)	7 (21.88%)	8 (28.57%)	8 (24.24%)
Number of participants with Blood Pressure Increased (AESIs)	2 (6.9%)	3 (9.38%)	1 (4%)	0 (%)	1 (3.13%)	2 (7.14%)	0 (%)
Number of participants with Cystitis (AESIs)	0 (%)	0 (%)	1 (4%)	2 (11.11%)	0 (%)	0 (%)	0 (%)
Number of participants with Dissociative reaction (AESIs)	11 (37.93%)	3 (9.38%)	4 (16%)	1 (5.56%)	4 (12.5%)	4 (14.29%)	4 (12.12%)
Number of participants with Memory gaps Amnesia (AESIs)	5 (17.24%)	0 (%)	1 (4%)	0 (%)	1 (3.13%)	0 (%)	0 (%)
Number of participants with QTc prolongation (AESIs)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (6.06%)
Number of participants with Sedation (AESIs)	4 (13.79%)	3 (9.38%)	1 (4%)	2 (11.11%)	2 (6.25%)	3 (10.71%)	0 (%)
Number of participants with Suicidality (AESIs)	2 (6.9%)	0 (%)	3 (12%)	3 (16.67%)	0 (%)	1 (3.57%)	2 (6.06%)

NOVARTIS

AUClast - Pharmacokinetics (PK) of MIJ821 in plasma

Description	AUClast of MIJ821 in plasma after 1st infusion. AUClast is the Area Under the Curve (AUC) from time zero to the last measurable concentration sampling time (tlast). Since PK was evaluated post the single first infusion, the bi-weekly and single dosing regimens of the same dose level are pooled as one arm for 0.048 mg/kg and 0.16 mg/kg.
Time Frame	Pre-dose, 20min, 40min, 4hours and 24hours post 1st infusion
Analysis Population Description	PK Analysis Set: included all participants who received MIJ821 and provided at least one evaluable measurement.

	MIJ821 0.16 mg/kg	**MIJ821 0.048 mg/kg**	**MIJ821 0.016 mg/kg**	**MIJ821 0.0048 mg/kg**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion
Number of Participants Analyzed [units: participants]	47	47	18	16
AUClast - Pharmacokinetics (PK) of MIJ821 in plasma (units: h*ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	347 ± 354	112 ± 123	28.4 ± 22.2	14.0 ± 23.9

Cmax - Pharmacokinetics (PK) of MIJ821 in plasma

Description	Cmax of MIJ821 in plasma after 1st infusion. AUClast is the maximum (peak) observed plasma, blood, serum, or other body fluid drug concentration after single dose administration. Since PK was evaluated post the single first infusion, the bi-weekly and single dosing regimens of the same dose level are pooled as one arm for 0.048 mg/kg and 0.16 mg/kg.
Time Frame	Pre-dose, 20min, 40min, 4hours and 24hours post 1st infusion
Analysis Population Description	PK Analysis Set: included all participants who received MIJ821 and provided at least one evaluable measurement.

	MIJ821 0.16 mg/kg	MIJ821 0.048 mg/kg	MIJ821 0.016 mg/kg	MIJ821 0.0048 mg/kg
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion
Number of Participants Analyzed [units: participants]	49	47	18	16
Cmax - Pharmacokinetics (PK) of MIJ821 in plasma (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	118 ± 177	25.4 ± 16.9	8.35 ± 6.67	6.02 ± 8.15

Number of participants meeting response criteria of ≥50% reduction in MADRS total score.

Description	Response criteria of ≥50% reduction from baseline in MADRS total score over time in the Core Period. 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 has a total possible score of 0 - 60. Higher scores represent a more severe condition.
Time Frame	6 weeks
Analysis Population Description	Full Analysis Set

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29

					Day 15 and Day 29	Day 15 and Day 29	
Number of Participants Analyzed [units: participants]	29	32	25	18	32	28	33
Number of participants meeting response criteria of ≥50% reduction in MADRS total score. (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Day 1, 4 Hours	10 (34.48%)	14 (43.75%)	7 (28%)	1 (5.56%)	8 (25%)	6 (21.43%)	16 (48.48%)
Day 2 (24 Hours)	8 (27.59%)	15 (46.88%)	12 (48%)	4 (22.22%)	13 (40.63%)	10 (35.71%)	14 (42.42%)
Day 8	10 (34.48%)	10 (31.25%)	11 (44%)	3 (16.67%)	9 (28.13%)	9 (32.14%)	13 (39.39%)
Day 15, Predose	12 (41.38%)	10 (31.25%)	9 (36%)	3 (16.67%)	10 (31.25%)	7 (25%)	10 (30.3%)
Day 15, 4 Hours	21 (72.41%)	23 (71.88%)	17 (68%)	7 (38.89%)	20 (62.5%)	17 (60.71%)	23 (69.7%)
Day 22	15 (51.72%)	17 (53.13%)	10 (40%)	5 (27.78%)	10 (31.25%)	8 (28.57%)	13 (39.39%)
Day 29, Predose	17 (58.62%)	16 (50%)	8 (32%)	7 (38.89%)	12 (37.5%)	10 (35.71%)	18 (54.55%)
Day 29, 4 Hours	21 (72.41%)	23 (71.88%)	19 (76%)	11 (61.11%)	21 (65.63%)	19 (67.86%)	23 (69.7%)
Day 36	15 (51.72%)	19 (59.38%)	14 (56%)	10 (55.56%)	18 (56.25%)	15 (53.57%)	21 (63.64%)
Day 43	19 (65.52%)	19 (59.38%)	17 (68%)	9 (50%)	17 (53.13%)	16 (57.14%)	22 (66.67%)

Number of participants meeting criteria for sustained response of ≥50% reduction in MADRS total score

Description Sustained response (≥50% reduction from baseline) from baseline in MADRS total score for a period of at least four weeks in the Core Period. 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 has a total possible score of 0 - 60. Higher scores represent a more severe condition.

Time Frame: 6 weeks

Analysis Population Description: Full Analysis Set

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Number of Participants Analyzed [units: participants]	29	32	25	18	32	28	33
Number of participants meeting criteria for sustained response of ≥50% reduction in MADRS total score (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	11 (37.93%)	11 (34.38%)	4 (16%)	3 (16.67%)	5 (15.63%)	4 (14.29%)	6 (18.18%)

NOVARTIS

Number of participants meeting remission criteria of MADRS total score of ≤12

Description	Remission criteria of MADRS total score of ≤12 over time in the Core Period. 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 has a total possible score of 0 - 60. Higher scores represent a more severe condition.
Time Frame	6 weeks
Analysis Population Description	Full Analysis Set

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Number of Participants Analyzed [units: participants]	29	32	25	18	32	28	33
Number of participants meeting remission criteria of MADRS total score of ≤12 (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Day 1, 4 Hours	4 (13.79%)	5 (15.63%)	2 (8%)	0 (%)	2 (6.25%)	4 (14.29%)	6 (18.18%)
Day 2 (24 Hours)	4 (13.79%)	8 (25%)	6 (24%)	1 (5.56%)	5 (15.63%)	7 (25%)	7 (21.21%)

Day 8	5 (17.24%)	5 (15.63%)	4 (16%)	1 (5.56%)	5 (15.63%)	2 (7.14%)	8 (24.24%)
Day 15, Predose	6 (20.69%)	4 (12.5%)	4 (16%)	1 (5.56%)	5 (15.63%)	2 (7.14%)	5 (15.15%)
Day 15, 4 Hours	13 (44.83%)	15 (46.88%)	10 (40%)	4 (22.22%)	10 (31.25%)	10 (35.71%)	16 (48.48%)
Day 22	9 (31.03%)	7 (21.88%)	3 (12%)	2 (11.11%)	8 (25%)	3 (10.71%)	10 (30.3%)
Day 29, Predose	8 (27.59%)	5 (15.63%)	4 (16%)	3 (16.67%)	6 (18.75%)	2 (7.14%)	12 (36.36%)
Day 29, 4 Hours	13 (44.83%)	18 (56.25%)	11 (44%)	6 (33.33%)	9 (28.13%)	11 (39.29%)	18 (54.55%)
Day 36	8 (27.59%)	12 (37.5%)	6 (24%)	3 (16.67%)	8 (25%)	4 (14.29%)	15 (45.45%)
Day 43	11 (37.93%)	10 (31.25%)	7 (28%)	6 (33.33%)	7 (21.88%)	5 (17.86%)	13 (39.39%)

Number of participants meeting sustained remission criteria of MADRS total score of ≤12

Description	Remission criteria of MADRS total score of ≤12 sustained for a period of at least four weeks in the Core Period. 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 has a total possible score of 0 - 60. Higher scores represent a more severe condition.
Time Frame	6 weeks
Analysis Population Description	Full Analysis Set

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose	Placebo
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes	MIJ821 0.048 mg/kg dose for 40 minutes IV	MIJ821 0.016 mg/kg dose for 40 minutes IV	MIJ821 0.0048 mg/kg dose for 40 minutes IV	MIJ821 0.16 mg/kg dose for 40 minutes IV	MIJ821 0.048 mg/kg dose for 40 minutes IV	40 minutes IV infusion of 0.9% sodium

	on Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	chloride on Day 1, Day 15 and Day 29
Number of Participants Analyzed [units: participants]	29	32	25	18	32	28	33
Number of participants meeting sustained remission criteria of MADRS total score of ≤12 (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	5 (17.24%)	3 (9.38%)	2 (8%)	2 (11.11%)	4 (12.5%)	1 (3.57%)	5 (15.15%)

Number of participants meeting criteria for relapse in the Extension Period

Description	For participants classified as responders in the core period who entered the extension period. Response is defined as a ≥ 50% reduction from the baseline MADRS score at any visit during the study. All participants meeting criteria for relapse over fixed period in the Extension Period. A relapse manifests as the appearance of new depressive symptoms or worsening of previously stable or improving MDD symptoms. During the Extension Period, participants experiencing deterioration must be assessed by the treating physician and the relapse must be confirmed by assessment with MADRS during scheduled or unscheduled visit.
Time Frame	From 6 weeks up to 58 weeks
Analysis Population Description	Responders/remitters who entered the 52 weeks extension period

	MIJ821 0.16 mg/kg bi-weekly	**MIJ821 0.048 mg/kg bi-weekly**	**MIJ821 0.016 mg/kg bi-weekly**	**MIJ821 0.0048 mg/kg bi-weekly**	**MIJ821 0.16 mg/kg single dose**	**MIJ821 0.048 mg/kg single dose**	**Placebo**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose	MIJ821 0.048 mg/kg dose for	MIJ821 0.016 mg/kg dose for	MIJ821 0.0048 mg/kg dose for	MIJ821 0.16 mg/kg dose for	MIJ821 0.048 mg/kg dose for	40 minutes IV infusion of

	for 40 minutes on Day 1, Day 15 and Day 29	40 minutes IV infusion on Day 1, Day 15 and Day 29	40 minutes IV infusion on Day 1, Day 15 and Day 29	40 minutes IV infusion on Day 1, Day 15 and Day 29	40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	0.9% sodium chloride on Day 1, Day 15 and Day 29
Number of Participants Analyzed [units: participants]	16	18	17	9	16	16	22
Number of participants meeting criteria for relapse in the Extension Period (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	7 (43.75%)	7 (38.89%)	10 (58.82%)	3 (33.33%)	5 (31.25%)	8 (50%)	10 (45.45%)

Number of relapsing participants meeting response criteria after the first retreatment infusion in the extension period

Description	Relapsing participants meeting response criteria or remission criteria after the first infusion of MIJ821 retreatment in the Extension Period. Response criteria (>=50% reduction from baseline in MADRS total score). Reinfusions are given at Day 1, 15 and 29 after relapse.
Time Frame	Up to 52 weeks after first retreatment infusion. Timepoints are relative to first retreatment (R) infusion for each patient, including Follow Up (F/U).
Analysis Population Description	Retreatment Set - included participants who received at least one dose for the retreatment of relapse. Participants who received Placebo in the core period received one of active MIJ821 treatment for the treatment of the relapse and are counted under the respective arm.

	MIJ821 0.16 mg/kg bi-weekly	**MIJ821 0.048 mg/kg bi-weekly**	**MIJ821 0.016 mg/kg bi-weekly**	**MIJ821 0.0048 mg/kg bi-weekly**	**MIJ821 0.16 mg/kg single dose**	**MIJ821 0.048 mg/kg single dose**
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on	MIJ821 0.048 mg/kg dose for 40 minutes IV	MIJ821 0.016 mg/kg dose for 40 minutes IV	MIJ821 0.0048 mg/kg dose for 40 minutes IV	MIJ821 0.16 mg/kg dose for 40 minutes IV	MIJ821 0.048 mg/kg dose for 40 minutes IV

	Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1, Day 15 and Day 29	infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29
Number of Participants Analyzed [units: participants]	9	8	9	2	7	10
Number of relapsing participants meeting response criteria after the first retreatment infusion in the extension period (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Day 1 R, 4 Hours	3 (33.33%)	5 (62.5%)	4 (44.44%)	0 (%)	1 (14.29%)	3 (30%)
Day 2 R (24 Hours)	5 (55.56%)	6 (75%)	6 (66.67%)	0 (%)	2 (28.57%)	5 (50%)
Day 8 R	5 (55.56%)	2 (25%)	2 (22.22%)	1 (50%)	2 (28.57%)	1 (10%)
Day 15 R, Predose	3 (33.33%)	4 (50%)	3 (33.33%)	0 (%)	2 (28.57%)	2 (20%)
Day 15 R, 4 Hours	4 (44.44%)	5 (62.5%)	7 (77.78%)	1 (50%)	2 (28.57%)	7 (70%)
Day 22 R	8 (88.89%)	6 (75%)	5 (55.56%)	1 (50%)	2 (28.57%)	2 (20%)
Day 29 R, Predose	6 (66.67%)	5 (62.5%)	4 (44.44%)	0 (%)	2 (28.57%)	2 (20%)
Day 29 R, 4 Hours	8 (88.89%)	6 (75%)	5 (55.56%)	2 (100%)	4 (57.14%)	6 (60%)
Day 36 R	8 (88.89%)	6 (75%)	5 (55.56%)	0 (%)	2 (28.57%)	5 (50%)
Day 43 R	7 (77.78%)	5 (62.5%)	6 (66.67%)	1 (50%)	4 (57.14%)	5 (50%)

Week 8 F/U R	1 (11.11%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Week 12 F/U R	1 (11.11%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (10%)
Week 16 F/U R	1 (11.11%)	3 (37.5%)	0 (%)	0 (%)	0 (%)	1 (10%)
Week 20 F/U R	2 (22.22%)	4 (50%)	2 (22.22%)	0 (%)	1 (14.29%)	4 (40%)
Week 24 F/U R	4 (44.44%)	4 (50%)	2 (22.22%)	0 (%)	2 (28.57%)	0 (%)
Week 28 F/U R	6 (66.67%)	2 (25%)	2 (22.22%)	1 (50%)	5 (71.43%)	2 (20%)
Week 32 F/U R	5 (55.56%)	1 (12.5%)	4 (44.44%)	1 (50%)	3 (42.86%)	0 (%)
Week 36 F/U R	4 (44.44%)	2 (25%)	5 (55.56%)	1 (50%)	3 (42.86%)	0 (%)
Week 40 F/U R	4 (44.44%)	2 (25%)	1 (11.11%)	1 (50%)	3 (42.86%)	0 (%)
Week 44 F/U R	5 (55.56%)	2 (25%)	2 (22.22%)	0 (%)	1 (14.29%)	2 (20%)
Week 48 F/U R	4 (44.44%)	1 (12.5%)	2 (22.22%)	0 (%)	2 (28.57%)	3 (30%)
Week 52 F/U R	3 (33.33%)	1 (12.5%)	1 (11.11%)	1 (50%)	3 (42.86%)	2 (20%)

Number of relapsing participants meeting remission criteria after the first retreatment infusion in the extension period

Description	Relapsing participants meeting response criteria or remission criteria after the first infusion of MIJ821 retreatment in the Extension Period. Remission criteria (MADRS total score <=12). Reinfusions are given at Day 1, 15 and 29 after relapse.
Time Frame	Up to 52 weeks after first retreatment infusion. Timepoints are relative to first retreatment (R) infusion for each patient, including Follow Up (F/U).

Analysis Population Description: Retreatment Set - included participants who received at least one dose for the retreatment of relapse. Participants who received Placebo in the core period received one of active MIJ821 treatment for the treatment of the relapse and are counted under the respective arm.

	MIJ821 0.16 mg/kg bi-weekly	MIJ821 0.048 mg/kg bi-weekly	MIJ821 0.016 mg/kg bi-weekly	MIJ821 0.0048 mg/kg bi-weekly	MIJ821 0.16 mg/kg single dose	MIJ821 0.048 mg/kg single dose
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29
Number of Participants Analyzed [units: participants]	9	8	9	2	7	10
Number of relapsing participants meeting remission criteria after the first retreatment infusion in the extension period (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Day 1 R, 4 Hours	2 (22.22%)	3 (37.5%)	2 (22.22%)	0 (%)	1 (14.29%)	1 (10%)
Day 2 R (24 Hours)	5 (55.56%)	6 (75%)	4 (44.44%)	0 (%)	2 (28.57%)	3 (30%)
Day 8 R	3 (33.33%)	2 (25%)	1 (11.11%)	0 (%)	2 (28.57%)	0 (%)
Day 15 R, Predose	2 (22.22%)	3 (37.5%)	2 (22.22%)	0 (%)	0 (%)	0 (%)
Day 15 R, 4 Hours	3 (33.33%)	4 (50%)	6 (66.67%)	1 (50%)	3 (42.86%)	6 (60%)

Day 22 R	5 (55.56%)	4 (50%)	3 (33.33%)	1 (50%)	1 (14.29%)	0 (%)
Day 29 R, Predose	4 (44.44%)	4 (50%)	2 (22.22%)	0 (%)	2 (28.57%)	0 (%)
Day 29 R, 4 Hours	7 (77.78%)	5 (62.5%)	5 (55.56%)	1 (50%)	4 (57.14%)	7 (70%)
Day 36 R	3 (33.33%)	3 (37.5%)	4 (44.44%)	1 (50%)	2 (28.57%)	2 (20%)
Day 43 R	6 (66.67%)	4 (50%)	5 (55.56%)	1 (50%)	3 (42.86%)	4 (40%)
Week 8 F/U R	1 (11.11%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Week 12 F/U R	1 (11.11%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (10%)
Week 16 F/U R	1 (11.11%)	3 (37.5%)	0 (%)	0 (%)	0 (%)	0 (%)
Week 20 F/U R	2 (22.22%)	3 (37.5%)	0 (%)	0 (%)	1 (14.29%)	2 (20%)
Week 24 F/U R	4 (44.44%)	4 (50%)	1 (11.11%)	0 (%)	2 (28.57%)	1 (10%)
Week 28 F/U R	3 (33.33%)	2 (25%)	1 (11.11%)	1 (50%)	5 (71.43%)	1 (10%)
Week 32 F/U R	4 (44.44%)	1 (12.5%)	2 (22.22%)	1 (50%)	3 (42.86%)	0 (%)
Week 36 F/U R	4 (44.44%)	2 (25%)	3 (33.33%)	1 (50%)	3 (42.86%)	0 (%)
Week 40 F/U R	4 (44.44%)	2 (25%)	1 (11.11%)	1 (50%)	3 (42.86%)	0 (%)
Week 44 F/U R	4 (44.44%)	2 (25%)	2 (22.22%)	0 (%)	1 (14.29%)	1 (10%)
Week 48 F/U R	4 (44.44%)	1 (12.5%)	2 (22.22%)	0 (%)	2 (28.57%)	1 (10%)

Week 52 F/U R	3 (33.33%)	1 (12.5%)	1 (11.11%)	1 (50%)	2 (28.57%)	2 (20%)

Other Pre-Specified Outcome Result(s)

Not applicable

Post-Hoc Outcome Result(s)

Not applicable

Safety Results

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of 58 weeks.
Additional Description	Placebo responders in the Core period who were followed up in the 52-week Extension period but required to be retreated due to a relapse were randomly switched to a MIJ821 regimen. For these participants AEs that occurred after start of treatment with MIJ821 are counted under the respective MIJ821 regimen.
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	MIJ821 0.16 mg/kg bi-	MIJ821 0.048 mg/kg bi-	MIJ821 0.016 mg/kg bi-	MIJ821 0.0048 mg/kg bi-	MIJ821 0.16 mg/kg single	MIJ821 0.048 mg/kg single	Placebo N = 33

	weekly N = 31	weekly N = 34	weekly N = 25	weekly N = 18	dose N = 34	dose N = 30	
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg bi-weekly dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.016 mg/kg bi-weekly dose in the extension period.	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.0048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg single dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg single dose in the extension period.	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Total Number Affected	0	0	0	0	0	0	1
Total Number At Risk	31	34	25	18	34	30	33

Serious Adverse Events

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of 58 weeks.
Additional Description	Placebo responders in the Core period who were followed up in the 52-week Extension period but required to be retreated due to a relapse were randomly switched to a MIJ821 regimen. For these participants AEs that occurred after start of treatment with MIJ821 are counted under the respective MIJ821 regimen.
Source Vocabulary for Table Default	MedDRA (26.0)

Collection Approach for Table Default Systematic Assessment

	MIJ821 0.16 mg/kg bi-weekly N = 31	MIJ821 0.048 mg/kg bi-weekly N = 34	MIJ821 0.016 mg/kg bi-weekly N = 25	MIJ821 0.0048 mg/kg bi-weekly N = 18	MIJ821 0.16 mg/kg single dose N = 34	MIJ821 0.048 mg/kg single dose N = 30	Placebo N = 33
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg bi-weekly dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.016 mg/kg bi-weekly dose in the extension period.	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.0048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg single dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg single dose in the extension period.	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Total # Affected by any Serious Adverse Event	5	7	6	4	4	5	8
Total # at Risk by any Serious Adverse Event	31	34	25	18	34	30	33
Cardiac disorders							

Cardiac arrest	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Psychiatric disorders							
Depression	1 (3.23%)	1 (2.94%)	2 (8.00%)	1 (5.56%)	1 (2.94%)	0 (0.00%)	1 (3.03%)
Depression suicidal	2 (6.45%)	1 (2.94%)	0 (0.00%)	1 (5.56%)	1 (2.94%)	1 (3.33%)	0 (0.00%)
Major depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Suicidal ideation	1 (3.23%)	3 (8.82%)	2 (8.00%)	2 (11.11%)	0 (0.00%)	0 (0.00%)	2 (6.06%)
Suicide attempt	1 (3.23%)	3 (8.82%)	3 (12.00%)	2 (11.11%)	1 (2.94%)	4 (13.33%)	5 (15.15%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of 58 weeks.
Additional Description	Placebo responders in the Core period who were followed up in the 52-week Extension period but required to be retreated due to a relapse were randomly switched to a MIJ821 regimen. For these participants AEs that occurred after start of treatment with MIJ821 are counted under the respective MIJ821 regimen.
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	MIJ821 0.16 mg/kg bi-weekly N = 31	MIJ821 0.048 mg/kg bi-weekly N = 34	MIJ821 0.016 mg/kg bi-weekly N = 25	MIJ821 0.0048 mg/kg bi-weekly N = 18	MIJ821 0.16 mg/kg single dose N = 34	MIJ821 0.048 mg/kg single dose N = 30	Placebo N = 33
Arm/Group Description	MIJ821 0.16 mg/kg i.v. dose for 40 minutes on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg bi-weekly dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.016 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.016 mg/kg bi-weekly dose in the extension period.	MIJ821 0.0048 mg/kg dose for 40 minutes IV infusion on Day 1, Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.0048 mg/kg bi-weekly dose in the extension period.	MIJ821 0.16 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.16 mg/kg single dose in the extension period.	MIJ821 0.048 mg/kg dose for 40 minutes IV infusion on Day 1 and 0.9% sodium chloride for 40 minutes IV infusion on Day 15 and Day 29. Including participants randomized to Placebo who switched to MIJ821 0.048 mg/kg single dose in the extension period.	40 minutes IV infusion of 0.9% sodium chloride on Day 1, Day 15 and Day 29
Total # Affected by any Other Adverse Event	25	27	18	13	20	29	19
Total # at Risk by any Other Adverse Event	31	34	25	18	34	30	33
Blood and lymphatic system disorders							
Anaemia	1 (3.23%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Iron deficiency anaemia	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leukopenia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Cardiac disorders							
Palpitations	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Sinus bradycardia	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinus tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Tachycardia	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Ear and labyrinth disorders							
Hypoacusis	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vertigo	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (10.00%)	0 (0.00%)
Endocrine disorders							
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Eye disorders							
Vision blurred	1 (3.23%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	1 (3.03%)
Abdominal pain upper	1 (3.23%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (3.03%)
Acid peptic disease	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Colitis	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	2 (6.45%)	1 (2.94%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Dental caries	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Diarrhoea	2 (6.45%)	5 (14.71%)	2 (8.00%)	1 (5.56%)	1 (2.94%)	1 (3.33%)	0 (0.00%)
Dry mouth	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Dyspepsia	1 (3.23%)	1 (2.94%)	2 (8.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Haemorrhoids	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hypoaesthesia oral	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Lip swelling	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	3 (9.68%)	2 (5.88%)	1 (4.00%)	3 (16.67%)	2 (5.88%)	2 (6.67%)	1 (3.03%)
Pancreatic steatosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Paraesthesia oral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Toothache	1 (3.23%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Vomiting	1 (3.23%)	0 (0.00%)	1 (4.00%)	1 (5.56%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions							
Asthenia	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (3.23%)	1 (2.94%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	2 (6.67%)	0 (0.00%)
Gait disturbance	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Illness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Infusion site extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Medical device site rash	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Pain	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral swelling	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.67%)	0 (0.00%)
Hepatobiliary disorders							
Hepatic steatosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (3.33%)	0 (0.00%)
Infections and infestations							
Bronchitis	0 (0.00%)	1 (2.94%)	1 (4.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Conjunctivitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.67%)	0 (0.00%)
COVID-19	2 (6.45%)	1 (2.94%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	2 (6.67%)	0 (0.00%)

Influenza	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	1 (3.23%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Otitis media	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paronychia	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Pneumonia	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.06%)
Respiratory tract infection viral	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	1 (3.23%)	1 (2.94%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications							
Contusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ligament sprain	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Overdose	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural erythema	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Investigations							
Amylase increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (3.33%)	0 (0.00%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (3.33%)	0 (0.00%)
Blood lactate dehydrogenase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)

Blood phosphorus decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Blood pressure diastolic increased	1 (3.23%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood pressure increased	1 (3.23%)	1 (2.94%)	1 (4.00%)	0 (0.00%)	1 (2.94%)	2 (6.67%)	0 (0.00%)
Blood pressure systolic increased	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
C-reactive protein increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gamma-glutamyltransferase increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Heart rate decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Heart rate increased	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic enzyme increased	1 (3.23%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (3.03%)
Liver function test increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Weight decreased	1 (3.23%)	2 (5.88%)	0 (0.00%)	1 (5.56%)	2 (5.88%)	0 (0.00%)	0 (0.00%)
Weight increased	3 (9.68%)	4 (11.76%)	5 (20.00%)	0 (0.00%)	2 (5.88%)	3 (10.00%)	5 (15.15%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders							
Dyslipidaemia	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Hyperkalaemia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperphagia	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertriglyceridaemia	0 (0.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Hyperuricaemia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Overweight	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (3.33%)	1 (3.03%)

Vitamin B12 deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Musculoskeletal and connective tissue disorders							
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (2.94%)	2 (6.67%)	0 (0.00%)
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (3.33%)	0 (0.00%)
Joint stiffness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	1 (2.94%)	1 (4.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)
Neck pain	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Osteoporosis	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Pain in jaw	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Renal hamartoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Nervous system disorders							
Akathisia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Amnesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Coordination abnormal	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Disturbance in attention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Dizziness	4 (12.90%)	4 (11.76%)	1 (4.00%)	2 (11.11%)	4 (11.76%)	4 (13.33%)	2 (6.06%)
Dysgeusia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dystonia	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	4 (12.90%)	10 (29.41%)	5 (20.00%)	3 (16.67%)	4 (11.76%)	7 (23.33%)	4 (12.12%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Lethargy	3 (9.68%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)

Memory impairment	5 (16.13%)	0 (0.00%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nerve compression	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychomotor hyperactivity	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sedation	1 (3.23%)	1 (2.94%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Sensory disturbance	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Somnolence	3 (9.68%)	2 (5.88%)	0 (0.00%)	1 (5.56%)	2 (5.88%)	4 (13.33%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Tremor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Tunnel vision	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders							
Agitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Anxiety	5 (16.13%)	1 (2.94%)	5 (20.00%)	2 (11.11%)	1 (2.94%)	2 (6.67%)	0 (0.00%)
Bradyphrenia	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Daydreaming	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Depersonalisation/derealisation disorder	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Depression	3 (9.68%)	3 (8.82%)	2 (8.00%)	3 (16.67%)	1 (2.94%)	3 (10.00%)	3 (9.09%)
Derealisation	1 (3.23%)	0 (0.00%)	0 (0.00%)	2 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dissociation	9 (29.03%)	3 (8.82%)	4 (16.00%)	0 (0.00%)	1 (2.94%)	4 (13.33%)	3 (9.09%)
Dissociative amnesia	3 (9.68%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (3.33%)	1 (3.03%)
Generalised anxiety disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Hypnagogic hallucination	1 (3.23%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Illusion	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Impulsive behaviour	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Initial insomnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Insomnia	6 (19.35%)	5 (14.71%)	3 (12.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	3 (9.09%)
Intentional self-injury	1 (3.23%)	1 (2.94%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	1 (3.33%)	1 (3.03%)
Irritability	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Logorrhoea	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Major depression	0 (0.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nightmare	0 (0.00%)	1 (2.94%)	1 (4.00%)	1 (5.56%)	2 (5.88%)	0 (0.00%)	0 (0.00%)
Panic attack	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Suicidal ideation	3 (9.68%)	1 (2.94%)	3 (12.00%)	1 (5.56%)	1 (2.94%)	4 (13.33%)	0 (0.00%)
Terminal insomnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders							
Dysuria	0 (0.00%)	0 (0.00%)	1 (4.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)
Micturition urgency	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proteinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Urinary hesitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders							
Breast cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Endometrial disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Galactorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Intermenstrual bleeding	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polymenorrhoea	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vulvovaginal pruritus	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders							
Bronchospasm	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Epistaxis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Hyperventilation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasal obstruction	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory symptom	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.33%)	0 (0.00%)
Skin and subcutaneous tissue disorders							
Dermatitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	1 (3.23%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin exfoliation	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Hypertension	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.03%)
Hypotension	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	1 (2.94%)	2 (6.67%)	2 (6.06%)
Phlebitis	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Relevant Findings

None

Conclusion:

The study failed to determine an efficacious dose at the end of the placebo-controlled core period and there was no dose-response relationship observed for all 4 doses of MIJ821 versus placebo. Therefore, the study did not meet its primary objective.

MIJ821 at the highest dose level 0.16 mg/kg bi-weekly showed sustained response, sustained remission and an effective reduction in severe suicidal symptoms in the participants. Mean MIJ821 Cmax and AUClast values increased with increasing dose. No impact on the systemic exposure was identified across all infusions per dose in Core and Retreatment period.

The safety and tolerability of MIJ821 was in line with the known safety profile of the drug, with no new safety concerns.

Date of Clinical Trial Report

Jul-17-2024