Clinical trial results:
Investigation of antidepressant efficacy of oral ketamine treatment

Summary

EudraCT number	2016-002068-14
Trial protocol	AT
Global end of trial date	13 October 2021

Results information

Result version number	v1 (current)
This version publication date	13 November 2025
First version publication date	13 November 2025
Summary attachment (see zip file)	Publication (Silberbauer 2025 ketamin oral depression.pdf)

Trial information

Trial identification

Sponsor protocol code	KET_po

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02992496
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Dpt of Psychiatry and Psychotherapy, Medical University of Vienna, 0043 14040035680, biol-psychiatry@meduniwien.ac.at
Scientific contact	Dpt of Psychiatry and Psychotherapy, Medical University of Vienna, 0043 14040035680, biol-psychiatry@meduniwien.ac.at

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	05 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2021
Global end of trial reached?	Yes
Global end of trial date	13 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the antidepressant efficacy of oral ketamine in patients suffering from a major depressive episode in a double-blinded randomized and controlled study design.

Protection of trial subjects:

Study risks were minimal and interventions were performed by trained clinical personnel. Side effects were monitored closely by standardized questionnaires.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 47
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	47
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients suffering from a depressive episode were recruited from the in- and outpatient clinic of the Department of Psychiatry and Psychotherapy, Medical University of Vienna. Patients were recruited between 24.04.2017 and 07.04.2021.

Pre-assignment

Screening details:

Stable psychopharmacological treatment for 10 days (except benzodiazepines) was required. Initiation of a new antidepressant/mood-stabilising treatment within 4 weeks prior to participation was an exclusion criterion. History of ketamine treatment, psychosis, or substance abuse within the past 12 months were further exclusion criteria.

Period 1

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

Blinding implementation details:

Randomization was performed by an independent researcher of our group not involved in the analysis or execution of the project. The randomization list was provided to the hospital pharmacy for preparation of the study medication. By using an active control treatment, unblinding due to unspecific drug effects was minimized. Further, adverse events were recorded by a different physician than the one responsible for assessment of depressive symptoms.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

Oral ketamine treatment 1mg/kg 6x over two weeks

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

1mg/kg applied per-orally at six occasions over the period of 12 days

Arm title	Midazolam

Arm description:

Oral midazolam treatment 0.03mg/kg 6x over two weeks

Arm type	Active comparator
Investigational medicinal product name	MIDAZOLAM HYDROCHLORIDE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

0.03 mg/kg applied per-orally at six occasions over 12 days

Number of subjects in period 1	Ketamine	Midazolam
Started	23	24
Completed	23	22
Not completed	0	2
Lost to follow-up	-	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Ketamine
Reporting group description: Oral ketamine treatment 1mg/kg 6x over two weeks	
Reporting group title	Midazolam
Reporting group description: Oral midazolam treatment 0.03mg/kg 6x over two weeks	

Primary: Depressive symptom score

End point title	Depressive symptom score
End point description: Change in MADRS score compared between treatment arms	
End point type	Primary
End point timeframe: baseline vs. 1 week after initiation of treatment	

End point values	Ketamine	Midazolam		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	22		
Units: MADRS				
arithmetic mean (standard deviation)	-7.695652 (± 10.87)	-5.772727 (± 9.24)		

Statistical analyses

Statistical analysis title	Mixed effects model for repeated measures
Statistical analysis description: An intention-to-treat analysis comprising all patients who received at least one dose was performed. A mixed effects model for repeated measures (baseline, 24 h, 7 days and 11 days after first dose) was calculated using maximum likelihood estimation. The intercept was allowed to vary randomly. Treatment group, time of visit and their interaction were included as fixed effects and subject as random effect.	
Comparison groups	Ketamine v Midazolam
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Administration of first dose until final examination scheduled at least 2 weeks after last dose	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	28.1

Reporting groups	
Reporting group title	Ketamine
Reporting group description: Oral ketamine treatment 1mg/kg 6x over two weeks	
Reporting group title	Midazolam
Reporting group description: Oral midazolam treatment 0.03mg/kg 6x over two weeks	

Serious adverse events	Ketamine	Midazolam	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Ketamine	Midazolam	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)	22 / 22 (100.00%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	6 / 23 (26.09%)	4 / 22 (18.18%)	
occurrences (all)	9	7	
Chest pain			
subjects affected / exposed	3 / 23 (13.04%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
Nervous system disorders			
Dizziness			

subjects affected / exposed	18 / 23 (78.26%)	8 / 22 (36.36%)	
occurrences (all)	29	13	
Headache			
subjects affected / exposed	7 / 23 (30.43%)	3 / 22 (13.64%)	
occurrences (all)	10	9	
Coordination abnormal			
subjects affected / exposed	12 / 23 (52.17%)	3 / 22 (13.64%)	
occurrences (all)	21	6	
Tremor			
subjects affected / exposed	2 / 23 (8.70%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Disturbance in attention			
subjects affected / exposed	15 / 23 (65.22%)	5 / 22 (22.73%)	
occurrences (all)	24	10	
General disorders and administration site conditions			
Hyperhidrosis			
subjects affected / exposed	7 / 23 (30.43%)	4 / 22 (18.18%)	
occurrences (all)	9	7	
Malaise			
subjects affected / exposed	8 / 23 (34.78%)	5 / 22 (22.73%)	
occurrences (all)	13	8	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	3 / 23 (13.04%)	3 / 22 (13.64%)	
occurrences (all)	5	4	
Eye disorders			
Vision blurred			
subjects affected / exposed	9 / 23 (39.13%)	4 / 22 (18.18%)	
occurrences (all)	17	8	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 23 (21.74%)	1 / 22 (4.55%)	
occurrences (all)	10	2	
Vomiting			
subjects affected / exposed	1 / 23 (4.35%)	0 / 22 (0.00%)	
occurrences (all)	1	0	

Dry mouth			
subjects affected / exposed	13 / 23 (56.52%)	8 / 22 (36.36%)	
occurrences (all)	22	12	
Constipation			
subjects affected / exposed	2 / 23 (8.70%)	1 / 22 (4.55%)	
occurrences (all)	3	2	
Diarrhoea			
subjects affected / exposed	1 / 23 (4.35%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 23 (4.35%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Dry skin			
subjects affected / exposed	4 / 23 (17.39%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	5 / 23 (21.74%)	2 / 22 (9.09%)	
occurrences (all)	6	4	
Psychiatric disorders			
Restlessness			
subjects affected / exposed	5 / 23 (21.74%)	5 / 22 (22.73%)	
occurrences (all)	9	9	
Anxiety			
subjects affected / exposed	7 / 23 (30.43%)	3 / 22 (13.64%)	
occurrences (all)	9	4	
Apathy			
subjects affected / exposed	7 / 23 (30.43%)	8 / 22 (36.36%)	
occurrences (all)	11	12	
Fatigue			
subjects affected / exposed	12 / 23 (52.17%)	11 / 22 (50.00%)	
occurrences (all)	19	22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported