Clinical trial results:
Positron Emission Tomography assessment of Ketamine Binding of the Serotonin Transporter and its Relevance for Rapid Antidepressant Response

Summary

EudraCT number	2014-003280-38
Trial protocol	AT
Global end of trial date	02 September 2020

Results information

Result version number	v1 (current)
This version publication date	13 December 2023
First version publication date	13 December 2023

Trial information

Trial identification

Sponsor protocol code	PSY-NIL-0006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02717052
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Währingergürtel 18-20, Vienna, Austria, 1090
Public contact	Univ. Prof. Rupert Lanzenberger, Department of Psychiatry and Psychotherapy, rupert.lanzenberger@meduniwien.ac.at
Scientific contact	Univ. Prof. Rupert Lanzenberger, Department of Psychiatry and Psychotherapy, rupert.lanzeberger@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	02 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2020
Global end of trial reached?	Yes
Global end of trial date	02 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study at hand is the first to investigate ketamine's serotonin transporter (SERT) binding in humans, by utilizing the highly selective SERT radioligand [11C]DASB and positron emission tomography (PET). Further, investigation of severely depressed patients provides the unique opportunity to establish the relationship between ketamine's SERT binding and its antidepressant efficacy. We aim to investigate
1. Does Esketamine Hydrochloride bind the SERT?*
2. Does binding of Esketamine Hydrochloride to the SERT predict antidepressant response?*

As part of amendments following changes were made:

Pilot studies:
PI. Does 0.50 mg/kg BW ketamine (racemic ketamine, ketamine Hameln) bind to the SERT (measured with PET)
PIII: Does 0.80 mg/kg BW ketamine (racemic ketamine, ketamine Hameln) bind to the SERT (measured with PET)**

Sub-study:
Sub: Does 0.80 mg/kg BW ketamine affect glutamate and GABA levels (measured with MRS)
*not assessed b/c pilot results were neg.
**not analysed

Protection of trial subjects:

Participants were observed by medical staff during the experimental procedures
Side effects were evaluated

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 2016
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: 77
Worldwide total number of subjects	77
EEA total number of subjects	77

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)	77
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was performed via local advertisement

Pre-assignment

Screening details:

Inclusion and exclusion criteria were assessed prior to inclusion.

Period 1

Period 1 title	Pilot study I, III, MRS substudy (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pilot I

Arm description:

0.5mg/kg bodyweight racemic ketamine (ketamine Hameln) diluted in 0.9% saline solution and applied intravenously with infusion pump

Arm type	Experimental
Investigational medicinal product name	Ketaminhydrochlorid (Ketamin hameln, 50mg/ml Ampullen; Hameln Pharma Plus GmbH; Sanova Pharma)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.5mg/kg bodyweight diluted in 0.9% saline solution, i.v., with infusion pump, over 40 min.

Arm title	Pilot III and MRS substudy

Arm description:

0.8mg/kg bodyweight racemic ketamine (ketamine Hameln) diluted in 0.9% saline solution and applied intravenously with infusion pump

Arm type	Experimental
Investigational medicinal product name	Ketaminhydrochlorid (Ketamin hameln, 50mg/ml Ampullen; Hameln Pharma Plus GmbH; Sanova Pharma)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.8mg/kg bodyweight diluted in 0.9% saline solution, i.v., with infusion pump, over 40 min.

Number of subjects in period 1	Pilot I	Pilot III and MRS substudy
Started	26	51
Completed	12	28
Not completed	14	23
Protocol deviation	14	23

Baseline characteristics

Reporting groups	
Reporting group title	Pilot study I, III, MRS substudy

Reporting group description: -

Reporting group values	Pilot study I, III, MRS substudy	Total	
Number of subjects	77	77	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	25.86		
standard deviation	± 4.51	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	77	77	

End points

End points reporting groups

Reporting group title	Pilot I
Reporting group description:	
0.5mg/kg bodyweight racemic ketamine (ketamine Hameln) diluted in 0.9% saline solution and applied intravenously with infusion pump	
Reporting group title	Pilot III and MRS substudy
Reporting group description:	
0.8mg/kg bodyweight racemic ketamine (ketamine Hameln) diluted in 0.9% saline solution and applied intravenously with infusion pump	
Subject analysis set title	Pilot I
Subject analysis set type	Per protocol
Subject analysis set description:	
Pilot I	
Subject analysis set title	MRS
Subject analysis set type	Per protocol
Subject analysis set description:	
Pilot III with MRS data and MRS substudy	
Subject analysis set title	Pilot I baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
Baseline PET	
Subject analysis set title	MRS baseline
Subject analysis set type	Per protocol
Subject analysis set description:	
baseline MRS	

Primary: SERT occupancy

End point title	SERT occupancy[1]
End point description:	
End point type	Primary
End point timeframe:	
PET 1 to PET 2	

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: This analysis is only performed for the Pilot I study

End point values	Pilot I	Pilot I	Pilot I baseline	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	12	12	
Units: Percent	12	12	12	

Statistical analyses

Statistical analysis title	Occupancy

Statistical analysis description:

(1-(BPND PET2/BPND PET1))*100

Comparison groups	Pilot I baseline v Pilot I
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.5
Method	descriptive

Other pre-specified: GABA+/tCr

End point title	GABA+/tCr[2]

End point description:

End point type	Other pre-specified

End point timeframe:

MRI1 to MRI2

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: This analysis is only performed for the MRS substudy and some pilot III subjects im whom MRS is available

End point values	Pilot III and MRS substudy	MRS	MRS baseline	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	25	
Units: arbitrary	25	25	25	

Statistical analyses

Statistical analysis title	repeated measures analyses of variance (rmANOVA)

Statistical analysis description:

Repeated measures analyses of variance (rmANOVA); metabolite (GABA+/tCr, Glx/tCr or GABA+/Glx) dependent variable, measurement (MRI1, MRI2) and ROI (thalamus, hippocampus, insula, putamen, rACC, cACC, PCC) within-subject factors, including interaction (measurement by region) and main effects (measurement, region) were tested.

Comparison groups	MRS v MRS baseline
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.5
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Entirety of study participation	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	2016
Reporting groups	
Reporting group title	Pilot I
Reporting group description: -	
Reporting group title	Pilot III and MRS
Reporting group description: -	

Serious adverse events	Pilot I	Pilot III and MRS	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Pilot I	Pilot III and MRS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	30 / 30 (100.00%)	
Cardiac disorders			
Hypertension			
subjects affected / exposed	2 / 12 (16.67%)	18 / 30 (60.00%)	
occurrences (all)	2	18	
Tachycardia			
subjects affected / exposed	3 / 12 (25.00%)	11 / 30 (36.67%)	
occurrences (all)	3	11	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	3 / 30 (10.00%) 3	
Psychiatric disorders Dissociation subjects affected / exposed occurrences (all)	12 / 12 (100.00%) 12	30 / 30 (100.00%) 30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2016	Added Ketanest S 25mg/ml Ampoules as study drug
08 June 2016	Added Pilot Study I and II
31 May 2017	Added Pilot Study III
13 September 2018	Added MRS substudy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported