Clinical trial results:
Ketamine augmentation of ECT to improve outcomes in depression

Summary

EudraCT number	2011-005476-41
Trial protocol	GB
Global end of trial date	30 September 2015

Results information

Result version number	v1 (current)
This version publication date	07 August 2020
First version publication date	07 August 2020
Summary attachment (see zip file)	Results summary (Final Report_Anderson Ketamine.pdf)

Trial information

Trial identification

Sponsor protocol code	MMHSCT1096

Additional study identifiers

ISRCTN number	ISRCTN14689382
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Former Manchester Mental Health and Social Care Trust
Sponsor organisation address	Bury New Road, Prestwich, United Kingdom, M25 3BL
Public contact	Annya Sekula, Greater Manchester Mental Health Trust, researchoffice@gmmh.nhs.uk
Scientific contact	Prof Ian Anderson, University of Manchester, 0044 0161 275 7428, ian.anderson@manchester.ac.uk

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	16 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2015
Global end of trial reached?	Yes
Global end of trial date	30 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the effectiveness of adjunctive glutamate antagonist Ketamine in mitigating the adverse effects of electroconvulsive therapy and optimize symptomatic improvement in depression.

Protection of trial subjects:

Patients excluded if had a history of drug or alcohol abuse, known hypersensitivity or contraindications to ketamine or excipients in the injection, significant cardiovascular disease, uncontrolled hypertension, glaucoma, cirrhosis or abnormal liver function, liver disease, known hypersensitivity or contraindications to concomitant medications used for ECT (propofol, suxamethonium), evidence of organic brain disease, pregnancy or risk of pregnancy.

Background therapy:

Oral psychotropic medication continued by the patient's medical team remained unchanged whee possible for at least the first 4 ECT treatments, and ideally until end of ECT.
Anaesthetic for their ECT course.

Evidence for comparator:

Placebo (saline) comparator, no active comparator. Saline used as an adjunct to patient's anaesthetic for their ECT course

Actual start date of recruitment	01 August 2012
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	United Kingdom: 79
Worldwide total number of subjects	79
EEA total number of subjects	79

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)	62
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

7 NHS Trusts involved(UK sites only). Recruitment started in December 2012. Last patient assessment was in June 2015.

Pre-assignment

Screening details:

In total 628 patients received ECT of whom 31% were potentially eligible for the study (47% were ineligible due to detention under the MHA). Of the 196 potentially eligible patients, 79 (40%) were randomised and 70 (36%) formed the final mITT sample (37 in the saline arm, 33 in the Ketamine arm). More: https://pubmed.ncbi.nlm.nih.gov/28359862/

Pre-assignment period milestones

Number of subjects started	79
Number of subjects completed	79

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

The patient, clinical team, ECT psychiatry team and investigator/assessor were blinded to the treatment arm. Only the anaesthetist was not blind. Dispensing was by prescription completed by the anaesthetist on study-approved forms that did not identify whether the drug is ketamine or normal saline and drew up by anaesthetist. ECT Clinic staff drug vials were dispensed boxed in plain packaging and the outer packaging 'labelled' as per Annex 13.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	N01AX03
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description:

Normal Saline bolus

Arm type	Placebo

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 1	Ketamine	Placebo
Started	40	39
Completed	33	37
Not completed	7	2
organisational reason	2	-
excluded post-randomisation (clinical reasons)	2	-
Medical contrainducation	-	1
Did not start ECT	3	1

Period 2

Period 2 title	Started ECT + Study Drug
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	AS1
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description:

Normal Saline bolus

Arm type	Placebo

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 2	Ketamine	Placebo
Started	33	37
Completed	33	36
Not completed	0	1
Consent withdrawn by subject	-	1

Period 3

Period 3 title	Mid-ECT
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	AS1
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description:

Normal Saline bolus

Arm type	Placebo
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:
Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 3	Ketamine	Placebo
Started	33	36
Completed	28	32
Not completed	5	4
Lost capacity	1	-
Consent withdrawn by subject	1	-
Lost to follow-up	2	3
Detained under MHA	1	1

Period 4	
Period 4 title	End of Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:
0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	AS1
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:
0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description:
Normal Saline bolus

Arm type	Placebo

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 4	Ketamine	Placebo
Started	28	32
Completed	25	23
Not completed	3	9
Consent withdrawn by subject	2	2
Other	-	1
Further ECT	1	2
Lost to follow-up	-	4

Period 5

Period 5 title	1 month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description:

0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	AS1
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description:

Normal Saline bolus

Arm type	Placebo

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 5	Ketamine	Placebo
Started	25	23
Completed	19	18
Not completed	6	5
Consent withdrawn by subject	-	1
Further ECT	2	1
Unavailable	1	-
Lost to follow-up	3	2
Detained under the MHA	-	1

Period 6	
Period 6 title	4 month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ketamine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ketamine hydrochloride
Investigational medicinal product code	N01AX03
Other name	
Pharmaceutical forms	Injection, Concentrate and solvent for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.5 mg/kg as an adjunct to anaesthetic for ECT, bolus.

Arm title	Placebo

Arm description: -

Arm type	Placebo

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection, Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Saline bolus as an adjunct to ECT anaesthetic.

Number of subjects in period 6	Ketamine	Placebo
Started	19	18
Completed	19	18

Baseline characteristics

Reporting groups	
Reporting group title	Ketamine
Reporting group description:	
0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description:	
Normal Saline bolus	

Reporting group values	Ketamine	Placebo	Total
Number of subjects	40	39	79
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52.5	56.4	
standard deviation	± 11.9	± 12.4	-
Gender categorical Units: Subjects			
Female	22	22	44
Male	18	17	35
Ethnicity Units: Subjects			
White	31	35	66
Other	9	4	13
Marital status Units: Subjects			
Married or current partner	13	19	32
Other	27	20	47
Illness Characteristics Units: Subjects			
Inpatient	11	21	32
Other	29	18	47
Illness Characteristics: Diagnosis Units: Subjects			
Bipolar disorder	4	7	11
Other	36	32	68
Illness characteristics: Previous ECT? Units: Subjects			
Yes	18	16	34
No	22	23	45
Illness characteristics: Family history of depression? Units: Subjects			
Yes	23	18	41
No	17	21	38
Illness characteristics: Family history of			

bipolar disorder Units: Subjects			
Yes	2	10	12
No	38	29	67
Current depressive episode: Melancholia no psychosis Units: Subjects			
Yes	26	25	51
No	14	14	28
Current depressive episode: Psychosis, with or without melancholia Units: Subjects			
Yes	3	8	11
No	37	31	68
Comorbidity: Anxiety disorder or secondary OCD Units: Subjects			
Yes	16	18	34
No	24	21	45
Comorbidity: Other psychiatric disorder Units: Subjects			
Yes	1	0	1
No	39	39	78
Comorbidity: Medical Illness Units: Subjects			
Yes	12	9	21
No	28	30	58
Psychotropic medication: SSRI Units: Subjects			
Yes	10	10	20
No	30	29	59
Psychotropic medication: SNRI Units: Subjects			
Yes	17	16	33
No	23	23	46
Psychotropic medication: TCA Units: Subjects			
Yes	4	7	11
No	36	32	68
Psychotropic medication: MAOI Units: Subjects			
Yes	0	1	1
No	40	38	78
Psychotropic medication: Other antidepressant Units: Subjects			
Yes	13	9	22
No	27	30	57
Psychotropic medication: Antipsychotic Units: Subjects			
Yes	21	25	46
No	19	14	33

Psychotropic medication: Lithium Units: Subjects			
Yes	10	5	15
No	30	34	64
Psychotropic medication: Antiepileptic mood stabiliser Units: Subjects			
Yes	5	6	11
No	35	33	68
Psychotropic medication: Hypnotic/anxiolytic Units: Subjects			
Yes	18	24	42
No	22	15	37
Mean years in full time education Units: Years			
arithmetic mean	13.7	13.5	
standard deviation	± 4.0	± 3.2	-
IQ Units: IQ score			
arithmetic mean	105.1	109.9	
standard deviation	± 11.3	± 11	-
MMSE Units: MMSE Score			
median	28.8	29.0	
standard deviation	± 2.0	± 1.2	-
Illness Characteristic: Age of onset Units: Years			
arithmetic mean	29.6	32.2	
standard deviation	± 14.0	± 17.0	-
Illness Characteristics: Number of Depressive episodes (lifetime) Units: Number			
median	4.9	5.3	
standard deviation	± 4.4	± 5.2	-
Illness Characteristics: number of hypomanic/manic episodes Units: Number			
median	0.3	0.5	
standard deviation	± 1.0	± 1.8	-
Current depressive episode: MADRS score Units: numeric score			
arithmetic mean	31.8	35.2	
standard deviation	± 7.4	± 8.4	-
Current depressive episode: Median duartion Units: Months			
median	14	8	
inter-quartile range (Q1-Q3)	7 to 38	3.5 to 20.5	-
Current depressive episode: MGHS score Units: Numeric score:			
median	4.8	4.0	

standard deviation	± 2.6	± 3.4	-
Physical signs: Weight			
Units: Kg			
arithmetic mean	82.2	77.2	
standard deviation	± 17.1	± 17.7	-
Physical signs: BMI			
Units: Kg/m2			
arithmetic mean	29.3	28.8	
standard deviation	± 5.8	± 6.7	-
Physical signs: Systolic blood pressure			
Units: mmHg			
arithmetic mean	132.9	126.1	
standard deviation	± 18.0	± 17.2	-

End points

End points reporting groups

Reporting group title	Ketamine
Reporting group description: 0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description: Normal Saline bolus	
Reporting group title	Ketamine
Reporting group description: 0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description: Normal Saline bolus	
Reporting group title	Ketamine
Reporting group description: 0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description: Normal Saline bolus	
Reporting group title	Ketamine
Reporting group description: 0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description: Normal Saline bolus	
Reporting group title	Ketamine
Reporting group description: 0.5mg Ketamine per kg, as an adjunct to anaesthetic for ECT.	
Reporting group title	Placebo
Reporting group description: Normal Saline bolus	
Reporting group title	Ketamine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: HVLT-R:Delayed Recall

End point title	HVLT-R:Delayed Recall
End point description:	
End point type	Primary
End point timeframe: Baseline to 4 month follow-up	

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	35
Units: Score				
median (standard deviation)	6.12 (± 2.69)	5.86 (± 3.63)	5.17 (± 2.92)	5.54 (± 3.42)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: Score				
median (standard deviation)	5.69 (± 2.80)	5.44 (± 3.18)	6.70 (± 2.67)	7.26 (± 2.63)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: Score				
median (standard deviation)	6.63 (± 3.17)	8.11 (± 2.83)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	0.87

Statistical analysis title	Repeated measures model analysis: end of treatment
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.94
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	1.13

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	0.6

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	0.12

Primary: HVLT-R: Total learning

End point title	HVLT-R: Total learning

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: HVLT-R Score				
arithmetic mean (standard deviation)	20.0 (± 4.1)	20.8 (± 6.7)	20.2 (± 5.8)	21.0 (± 5.4)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: HVLT-R Score				
arithmetic mean (standard deviation)	19.8 (± 4.9)	21.2 (± 5.6)	22.3 (± 4.7)	23.5 (± 5.6)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: HVLT-R Score				
arithmetic mean (standard deviation)	21.6 (± 5.0)	24.1 (± 6.1)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	Repeated measures model analysis
Parameter estimate	Median difference (final values)
Point estimate	-0.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	1.81

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.97
upper limit	1.06

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	1.54

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.39
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.68
upper limit	1.44

Primary: HVLT-R: Retention

End point title	HVLT-R: Retention

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	35
Units: HVLT-R Score				
arithmetic mean (standard deviation)	73.3 (± 27.8)	65.2 (± 32.9)	58.6 (± 25.0)	62.4 (± 31.8)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: HVLT-R Score				
arithmetic mean (standard deviation)	69.4 (± 26.6)	58.7 (± 26.4)	73.3 (± 24.0)	77.1 (± 16.1)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: HVLT-R Score				
arithmetic mean (standard deviation)	74.72 (± 23.3)	85.5 (± 18.7)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	7.8

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	6.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.88
upper limit	18.8

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-3.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	6.9

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-11.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24
upper limit	0.1

Primary: HVLT-R: Recognition discrimination

End point title	HVLT-R: Recognition discrimination

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	35
Units: HVLT-R score				
arithmetic mean (standard deviation)	9.45 (± 2.05)	8.16 (± 3.48)	8.48 (± 2.81)	8.54 (± 2.84)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: HVLT-R score				
arithmetic mean (standard deviation)	8.58 (± 2.90)	9.66 (± 2.10)	9.52 (± 2.33)	9.52 (± 2.33)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: HVLT-R score				
arithmetic mean (standard deviation)	10.42 (± 1.43)	9.56 (± 2.97)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	0.44

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	-0.42

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	0.43

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	1.8

Primary: COWAT: Letter Fluency

End point title	COWAT: Letter Fluency

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: COWAT Score				
arithmetic mean (standard deviation)	33.8 (± 13.1)	36.1 (± 14.3)	31.5 (± 2.91)	36.1 (± 13.2)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: COWAT Score				
arithmetic mean (standard deviation)	33.0 (± 13.4)	34.2 (± 13.5)	35.6 (± 13.4)	39.5 (± 14.1)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: COWAT Score				
arithmetic mean (standard deviation)	37.6 (± 13.2)	38.6 (± 10.7)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.86
upper limit	2.23

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.57
upper limit	3.54

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.74
upper limit	2.7

Statistical analysis title	Repeated measures analysis: 4 moth follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.94
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	4.8

Primary: COWAT: Category Fluency

End point title	COWAT: Category Fluency

End point description:

End point type	Primary

End point timeframe:

Baseline to follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: COWAT Score				
arithmetic mean (standard deviation)	15.8 (± 5.5)	16.8 (± 5.3)	15.9 (± 5.3)	16.4 (± 4.2)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: COWAT Score				
arithmetic mean (standard deviation)	14.3 (± 5.1)	15.8 (± 4.2)	16.5 (± 5.6)	17.1 (± 4.1)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: COWAT Score				
arithmetic mean (standard deviation)	17.8 (± 4.6)	18.1 (± 5.3)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	1.78

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Placebo v Ketamine
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.15
upper limit	0.57

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	1.96

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	2.21

Primary: AMI-SF

End point title	AMI-SF

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: AMI-SF score				
arithmetic mean (standard deviation)	45.5 (± 9.2)	44.2 (± 10.3)	39.3 (± 9.0)	38.0 (± 10.0)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	32	23	23
Units: AMI-SF score				
arithmetic mean (standard deviation)	34.7 (± 9.8)	34.8 (± 10.5)	35.1 (± 10.0)	35.4 (± 10.4)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	16		
Units: AMI-SF score				
arithmetic mean (standard deviation)	37.4 (± 10.1)	38.9 (± 8.4)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.16
upper limit	1.81

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.95
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.63
upper limit	3.41

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.91
upper limit	3

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.93
upper limit	2.54

Primary: MCGCFT: Copy	
End point title	MCGCFT: Copy
End point description:	

End point type	Primary
End point timeframe:	
Baseline to 4 month follow-up	

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: MCGCFT Score				
arithmetic mean (standard deviation)	34.6 (± 2.4)	33.4 (± 4.3)	33.9 (± 4.0)	34.1 (± 3.2)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: MCGCFT Score				
arithmetic mean (standard deviation)	34.6 (± 2.0)	34.4 (± 2.4)	35.3 (± 1.2)	34.4 (± 3.0)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: MCGCFT Score				
arithmetic mean (standard deviation)	35.2 (± 1.1)	35.0 (± 1.1)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.27
upper limit	0.96

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	0.57

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	0.78

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.32
upper limit	0.34

Primary: MCGCFT: Immediate recall	
End point title	MCGCFT: Immediate recall
End point description:	

End point type	Primary
End point timeframe:	
Baseline to 4 month follow-up	

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: MCGCFT Score				
arithmetic mean (standard deviation)	19.0 (± 8.8)	17.9 (± 7.6)	18.6 (± 8.6)	18.4 (± 7.2)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: MCGCFT Score				
arithmetic mean (standard deviation)	19.0 (± 7.4)	16.6 (± 6.2)	19.5 (± 6.0)	19.7 (± 6.7)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: MCGCFT Score				
arithmetic mean (standard deviation)	23.8 (± 8.1)	21.5 (± 6.4)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.09
upper limit	2.39

Statistical analysis title	Repeated measures analysis: End of Treatment
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.61
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.77
upper limit	3

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.43
upper limit	0.5

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.05
upper limit	3.58

Primary: MCGCFT: Delayed recall

End point title	MCGCFT: Delayed recall

End point description:

End point type	Primary

End point timeframe:

Baseline to 4 month follow-up

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	29	35
Units: MCGCFT Score				
arithmetic mean (standard deviation)	18.9 (± 7.7)	17.6 (± 6.9)	17.7 (± 8.2)	17.7 (± 7.5)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	32	22	23
Units: MCGCFT Score				
arithmetic mean (standard deviation)	17.6 (± 5.9)	15.3 (± 5.3)	18.9 (± 6.4)	19.0 (± 6.5)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: MCGCFT Score				
arithmetic mean (standard deviation)	22.9 (± 9.7)	20.8 (± 6.8)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	2.1

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.85
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	2.36

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	0.37

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.89
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.79
upper limit	4.36

Primary: Digit span: Forward	
End point title	Digit span: Forward
End point description:	

End point type	Primary
End point timeframe:	
Baseline to follow-up	

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: Digits				
arithmetic mean (standard deviation)	5.70 (± 1.07)	5.84 (± 1.07)	5.48 (± 0.95)	6.0 (± 1.04)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: Digits				
arithmetic mean (standard deviation)	5.88 (± 1.34)	5.84 (± 1.02)	5.91 (± 1.04)	5.83 (± 1.11)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: Digits				
arithmetic mean (standard deviation)	5.68 (± 1.20)	5.72 (± 0.89)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.11

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Placebo v Ketamine
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.5

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.46

Statistical analysis title	Repeated measures analysis: 4 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.27

Secondary: Digit Span: Backwards

End point title	Digit Span: Backwards
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to follow-up	

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	37	29	36
Units: Digits				
arithmetic mean (standard deviation)	3.64 (± 1.17)	3.95 (± 1.10)	3.86 (± 1.38)	3.94 (± 1.01)

End point values	Ketamine	Placebo	Ketamine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	32	23	23
Units: Digits				
arithmetic mean (standard deviation)	3.88 (± 1.21)	3.97 (± 0.97)	3.87 (± 1.25)	4.13 (± 1.29)

End point values	Ketamine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: Digits				
arithmetic mean (standard deviation)	3.89 (± 1.05)	4.06 (± 1.06)		

Statistical analyses

Statistical analysis title	Repeated measures analysis: Mid-ECT
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.59

Statistical analysis title	Repeated measures analysis: End of treatment
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.42

Statistical analysis title	Repeated measures analysis: 1 month follow-up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.43

Statistical analysis title	Repeated measures analysis: 4 month follow up
Comparison groups	Ketamine v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Repeated measures model analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 4 month follow-up. Time frame for ARs during administration of IMP

Adverse event reporting additional description:

Safety was monitored by standard clinical procedures during ECT treatments, degree of re-orientation 30min after ECT, and adverse event recording.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Ketamine

Reporting group description:

Ketamine 0.5mg/kg as an adjunct to anaesthetic for ECT.

Reporting group title	Placebo

Reporting group description:

Normal saline bolus

Serious adverse events	Ketamine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 33 (6.06%)	5 / 37 (13.51%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Overdose	Additional description: Placebo-overdose requiring treatment in accident and emergency department Ketamine- overdose requiring treatment in accident and emergency department		
subjects affected / exposed	1 / 33 (3.03%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Chest pain	Additional description: chest pain requiring admission to hospital overnight		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizures	Additional description: spontaneous seizure and status epilepticus between ETC treatments		

subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt	Additional description: Suicide attempt requiring general hospital admission.		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt with intervention	Additional description: Suicide attempt on in patient ward requiring intervention		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
psychiatric deterioration	Additional description: clinical deterioration with suicidal ideation requiring admission to hospital		
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ketamine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 33 (66.67%)	10 / 37 (27.03%)	
Vascular disorders			
Vascular disorders	Additional description: Vascular disorders		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder	Additional description: Respiratory, thoracic and mediastinal disorders		
subjects affected / exposed	1 / 33 (3.03%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Psychiatric disorders			
Psychiatric disorders	Additional description: Psychiatric disorders		
subjects affected / exposed	7 / 33 (21.21%)	6 / 37 (16.22%)	
occurrences (all)	7	6	
Cardiac disorders			

Cardiac disorders	Additional description: Cardiac disorders		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Nervous system disorders			
Nervous system disorder	Additional description: Nervous system disorder		
subjects affected / exposed	4 / 33 (12.12%)	1 / 37 (2.70%)	
occurrences (all)	4	1	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: Blood and lymphatic system disorder		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Eye disorders			
Eye disorders	Additional description: Eye disorders		
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: Gastrointestinal disorders		
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: Hepatobiliary disorders		
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorder	Additional description: Skin and subcutaneous tissue disorder		
subjects affected / exposed	2 / 33 (6.06%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Renal and urinary disorders	Additional description: Renal and urinary disorders		
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal disorder	Additional description: Musculoskeletal and connective tissue disorder		
subjects affected / exposed	3 / 33 (9.09%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			

Infections and infestations	Additional description: Infections and infestations		
subjects affected / exposed	3 / 33 (9.09%)	0 / 37 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2012	Protocol changed to implement: -Change of timing of primary outcome and MR imaging -Definition clarified of timing of primary outcome (after 4th ECT subject to SOP defined variation) and end of ECT -Modification/addition of some assessments -Change of timing of ketamine administration to before the anaesthetic induction agent which has now been limited to propofol only -Addition of sample for DNA

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.

Recruitment under 50%. In the fNIRS sub-study the effect of ketamine could not be assessed and the other findings must be viewed as preliminary. Included patients were younger, with limited cognitive impairment with ECT which limits generalisation.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28359862