



Clinical trial results:

A randomized , double-blind, placebo-controlled study of antidepressant effects of the endogen compound neuropeptide y (NPY) in patients suffering from major depressive disorder

Summary

EudraCT number	2014-000129-19
Trial protocol	SE
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	26 October 2022
First version publication date	26 October 2022
Summary attachment (see zip file)	Abstract (NPY abstract one.docx) NPY abstract on (NPY 2020 crucial pyaa054.pdf) MIRANDA npy attachment one (MIRANDA npy attachment one.docx)

Trial information

Trial identification

Sponsor protocol code	NPY
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska Institute, d
Sponsor organisation address	Solnavägen 1, Stockholm, Sweden, 17177
Public contact	Aleksander Mathé, MD, PhD, Senior Professor, Karolinska University Hospital, Huddinge, +46 704840743, aleksander.mathe@ki.se
Scientific contact	Aleksander Mathé, MD, PhD, Senior Professor, Karolinska University Hospital, Huddinge, +46 704840743, aleksander.mathe@ki.se

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	Interim
Date of interim/final analysis	14 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2020
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

study if NPY decreases symptoms of depression

Protection of trial subjects:

Institutional review board (EPN, Regionala Etikprövningsnämnden i Stockholm, Dnr 2014/582- 31/2 and 2015/1233-32)

Background therapy:

none

Evidence for comparator: -

Actual start date of recruitment	01 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited by the Karolinska Trial Alliance via advertisement, who also monitored the trial. All participants signed the informed consent form.

Pre-assignment

Screening details:

At the screening visit, participants met the study physician who took the medical history and performed a physical examination. ECG and vital signs were recorded; urine toxicology and an alcohol breath test were taken. Safety blood samples were drawn and a pregnancy test taken. Prior and concomitant medications were documented. Nov-15 to Oct-17

Pre-assignment period milestones

Number of subjects started	30
Number of subjects completed	30

Period 1

Period 1 title	Trial (overall period)
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 list of random treatment assignments was set up according to the random permuted blocks method with blocks of 10 patients. NPY and placebo were prepared by an independent person not otherwise involved in any of the study procedures. A randomization list was only available to the independent person preparing the study drug. All other study personnel were blind to treatment assignment. Code envelopes were available at the study site in case the treatment blind needed to be broken for emergency

Arms

Are arms mutually exclusive?	Yes
Arm title	NPY experimental drug

Arm description:

NPY

Arm type	Experimental
Investigational medicinal product name	NPY
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Intranasal use

Dosage and administration details:

s. On the day of the experiment, the designated pharmacist who was not otherwise involved in any of the study procedures (APL, Pharmacy, Steriltillverkningen Karolinska Solna) prepared the NPY (6,8 mg) or placebo in sterile water and delivered the unmarked syringes to the person responsible for experimental solution administration with the ViaNase Electronic Atomizer (Kurve Technology Inc, Bothel, WA).

Arm title	Placebo
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Arm description:

Placebo intranasal spray

Arm type	Placebo
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Investigational medicinal product name	sterile water
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Intranasal use

Dosage and administration details:

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Number of subjects in period 1	NPY experimental drug	Placebo
Started	12	18
Completed	12	18

Baseline characteristics

Reporting groups

Reporting group title	Trial
Reporting group description:	
NPY and Placebo	

Reporting group values	Trial	Total	
Number of subjects	30	30	
Age categorical			
Median 57.0 (NPY), 52.8 (placebo)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	55		
standard deviation	± 13	-	
Gender categorical			
20 Female, 10 Male			
Units: Subjects			
Female	20	20	
Male	10	10	
MADRS			
Median 30,2 (NPY), 28,1 (placebo)			
Units: Subjects			
MADRS	30	30	

End points

End points reporting groups

Reporting group title	NPY experimental drug
Reporting group description:	
NPY	
Reporting group title	Placebo
Reporting group description:	
Placebo intranasal spray	
Subject analysis set title	MADRS
Subject analysis set type	Full analysis

Subject analysis set description:

Primary Outcome: MADRS—Changes in MADRS score by group within the 48 hours post NPY insufflation are presented in Figure 1 and Tables 2 and 3. NPY was superior to placebo in reducing MADRS score at 24 hours posttreatment; decrease of 10.3 points (95% CI: −13.5; −6.8) vs decrease of 5.6 points (95% CI: −8.4; −2.7), respectively (group*time interaction $F=3.26$ $DF=(1,28)$, $P=.04$; Cohen's $d=0.67$). There was a similar trend toward benefit of NPY over placebo at +1 hour (decrease of 5.7 points [95% CI: −8.5; −2.8] vs decrease of 3.8 points [95% CI: −6.2; −1.5]; group*time interaction $F = 0.71$ $DF = (1,28)$, $P = .20$) and at +5 hours (decrease of 7.1 points [95% CI −10.0; −4.2] vs decrease of 3.5 points [95% CI: −5.8; −1.2]; group*time interaction $F=2.69$, $DF=(1,28)$, $P=.05$; Cohen's $d=0.61$). At +48 hours there was no longer a separation between NPY and placebo (decrease of 8.3 [95% CI: −12.5; −4.3] vs 8.5 points [95% CI: −11.8; −5.2]; group*time interaction $F = 0.0001$, $DF = (1,28)$, $P = .49$).

Primary: 24 h post inhalation

End point title	24 h post inhalation
End point description:	
End point type	Primary
End point timeframe:	
24 hours after inhalation	

End point values	NPY experimental drug	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[1]	18 ^[2]		
Units: Points in MADRS				
number (confidence interval 95%)	10.3 (6.8 to 13.5)	5.6 (2.7 to 8.4)		

Notes:

[1] - NPY

[2] - Placebo

Statistical analyses

Statistical analysis title	MADRS
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Statistical analysis description:

Analytic approach—Two-way ANOVA for repeated measures, Mann-Whitney U test, and Wilcoxon Matched Pairs test were used. Homogeneity of variances was examined using boxplots and Levene's test. $P<.05$ was considered significant. Since this was designed as an early-phase proof of concept study,

there was no adjustment planned for multiplicity.

Comparison groups	Placebo v NPY experimental drug
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.5
Method	ANOVA
Parameter estimate	Median difference (final values)

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Duration of experiment, 5 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no adverse events recorded during the course of the trial

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

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

Enrollment ended early, at n=30, due to un-anticipated limitation of drug supply
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Notes: