Clinical trial results:
The efficacy of transcranial direct current stimulation (tDCS) in the treatment of depression and brain functional changes compared to venlafaxine.

Summary

EudraCT number	2015-001639-19
Trial protocol	CZ
Global end of trial date	24 April 2019

Results information

Result version number	v1 (current)
This version publication date	29 July 2021
First version publication date	29 July 2021

Trial information

Trial identification

Sponsor protocol code	15-29900A

Additional study identifiers

ISRCTN number	ISRCTN93220632
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Narodní ústav duševního zdraví
Sponsor organisation address	Topolova 748, Klecany, Czechia, 25067
Public contact	2nd Dpt. of the Clinical Division, Národní ústav duševního zdraví, Martin.Bares@nudz.cz
Scientific contact	2nd Dpt. of the Clinical Division, Národní ústav duševního zdraví, Martin.Bares@nudz.cz

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	24 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2019
Global end of trial reached?	Yes
Global end of trial date	24 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of 4-week, double-blind and subsequent 8-week, open-label studies is to compare efficacy and tolerability of transcranial direct
current stimulation and venlafaxine in the acute treatment of depression and relapse prevention.

Protection of trial subjects:

No

Background therapy:

Hydroxyzine up to 100 mg; Zolpidem 10 mg - rescue treatment

Evidence for comparator:

Venlafaxine as a first line treatment of depressive disorder according to international guidelines for treatment of depression.

Actual start date of recruitment	03 August 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	57

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All territories of the Czech Republic, from October 2015 to March 2019

Pre-assignment

Screening details:

initial wash out period 2–7 days; assessed for eligibility 323, randomized 57, not meet inclusion criteria 200, declined to participate 62, other reasons 4

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	Investigator, Monitor, Data analyst, Subject

Blinding implementation details:

No

Arms

Are arms mutually exclusive?	Yes
Arm title	VNF+sham

Arm description:

venlafaxine + sham direct current stimulation (tDCS)

Arm type	Active comparator
Investigational medicinal product name	Venlafaxin Mylan 75 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

75 - 375 mg per day

Arm title	tDCS

Arm description:

transcranial direct current stimulation + placebo capsules

Arm type	Experimental
Investigational medicinal product name	placebo capsules
Investigational medicinal product code	
Other name	placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1-5 capsules a day

Number of subjects in period 1	VNF+sham	tDCS
Started	28	29
baseline	28	29
Completed	22	23
Not completed	6	6
Consent withdrawn by subject	2	1
Adverse event, non-fatal	-	1
Lack of efficacy	4	4

Baseline characteristics

Reporting groups	
Reporting group title	VNF+sham
Reporting group description:	
venlafaxine + sham direct current stimulation (tDCS)	
Reporting group title	tDCS
Reporting group description:	
transcranial direct current stimulation + placebo capsules	

Reporting group values	VNF+sham	tDCS	Total
Number of subjects	28	29	57
Age categorical			
No additional details			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	29	57
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44.6	46.6	
standard deviation	± 11.7	± 13.0	-
Gender categorical			
Units: Subjects			
Female	19	17	36
Male	9	12	21
treatment resistance			
number of subjects who did not respond at least two prevous antidepressant trial			
Units: Subjects			
resistant	11	11	22
non-resistant	17	18	35
number of previous depressive epizodes			
number of previous depressive epizodes in subject´s life			
Units: number			
arithmetic mean	2.1	1.6	
standard deviation	± 1.8	± 1.8	-
illness duration (months)			
illness duration (months)			
Units: months			
arithmetic mean	98.3	82.9	
standard deviation	± 83.4	± 90.9	-

End points

End points reporting groups	
Reporting group title	VNF+sham
Reporting group description: venlafaxine + sham direct current stimulation (tDCS)	
Reporting group title	tDCS
Reporting group description: transcranial direct current stimulation + placebo capsules	
Subject analysis set title	efficacy analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description: all randomized patients who received at least one dose or stimulation of allocated treatment	

Primary: a change in the MADRS	
End point title	a change in the MADRS
End point description:	
End point type	Primary
End point timeframe: 4 weeks	

End point values	VNF+sham	tDCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	29		
Units: point				
arithmetic mean (confidence interval 95%)	9.64 (6.20 to 13.09)	7.69 (5.09 to 10.29)		

Statistical analyses

Statistical analysis title	efficacy analyses
Comparison groups	VNF+sham v tDCS
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided

Statistical analysis title	efficacy
Comparison groups	VNF+sham v tDCS

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	6.16

Secondary: remission rate

End point title	remission rate
End point description: MADRS score lower or equal to 10 points at week 4	
End point type	Secondary
End point timeframe: 4 weeks	

End point values	VNF+sham	tDCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	29		
Units: number				
number (not applicable)	9	5		

Statistical analyses

Statistical analysis title	comparison of remission rates between groups
Comparison groups	VNF+sham v tDCS
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: overal trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
Reporting groups	
Reporting group title	VNF+sham
Reporting group description: venlafaxine + sham direct current stimulation (tDCS)	
Reporting group title	tDCS
Reporting group description: transcranial direct current stimulation + placebo capsules	

Serious adverse events	VNF+sham	tDCS	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	1 / 29 (3.45%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
mania			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	VNF+sham	tDCS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 28 (60.71%)	20 / 29 (68.97%)	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 28 (39.29%)	10 / 29 (34.48%)	
occurrences (all)	50	40	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	15 / 28 (53.57%)	15 / 29 (51.72%)	
occurrences (all)	15	15	
Insomnia			
subjects affected / exposed	12 / 28 (42.86%)	12 / 29 (41.38%)	
occurrences (all)	20	20	
sleepiness			
subjects affected / exposed	17 / 28 (60.71%)	19 / 29 (65.52%)	
occurrences (all)	35	40	

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.

no

Notes: