Clinical trial results:
Effect of dexmedetomidine vs propofol on basal ganglia activity (local field potentials) recorded through implanted stimulators

Summary

EudraCT number	2014-000868-17
Trial protocol	ES
Global end of trial date	18 December 2015

Results information

Result version number	v1 (current)
This version publication date	24 November 2021
First version publication date	24 November 2021

Trial information

Trial identification

Sponsor protocol code	DEXPROPAR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02256319
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clinica Universidad de Navarra
Sponsor organisation address	AVENIDA PÍO XII, Nº 36, PAMPLONA/IRUÑA, Spain, 31008
Public contact	UCICEC, Clinica Universidad de Navarra, 34 948 255 400, ucicec@unav.es
Scientific contact	UCICEC, Clinica Universidad de Navarra, 34 948 255 400, ucicec@unav.es

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 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2015
Global end of trial reached?	Yes
Global end of trial date	18 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Study whether there are changes (and their characteristics) in local field potentials recordings in deep subcortical structures, obtained through the stimulators implanted to treat Parkinson's disease, with the administration of dexmedetomidine and propofol.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2014
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	Spain: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	8
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

12 patiens, 18 Years and older.

Pre-assignment

Screening details:

This clinical trial has been designed to study and compare changes in deep brain activity (field potentials) in Parkinson's disease (PD) patients while awake, and during sedation with dexmedetomidine or propofol.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Treatment

Arm description:

Experimental: Dexmedetomidine recording
Recording registered through the deep brain stimulation electrodes with dexmedetomidine at 0.2 µg/kg/h.
Intervention: Drug: Dexmedetomidine

Active Comparator: Propofol recording
Recording registered through the deep brain stimulation electrodes with propofol at plasmatic levels of 0.5, 1, 1.5, 2, 2.5 µg/mL.
Intervention: Drug: Propofol

No Intervention: Basal recording
Recording registered through the deep brain stimulation electrodes with no sedation .

Arm type	Experimental
Investigational medicinal product name	DEXMEDETOMIDINE
Investigational medicinal product code	
Other name	(S)-4-[1-(2,3-Dimethylphenyl)ethyl]-3H-imidazole
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients will receive a loading dose of 1 µg/kg in 10 min before starting the surgery. The maintenance dose will be 0.2-1 µg/kg/h for a Ramsey Sedation Score of 3-4 during the surgery´s preparation. It will be reduced to 0.2 µg/kg/h 15 min before starting the microelectrode recording for a Ramsey Sedation Score of 2. After the placement of the deep brain stimulator we will record the local field potentials activity. In addition, the subscales of rigidity, tremor and bradykinesia of the Unified Parkinson's Disease Rating Scale (UPDRS-III) score will be evaluated. Once the deep brain stimulator recording and neurologic exploration will be over patients will receive a maintenance dose 0.2-1 µg/kg/h until the end of the surgery. It will be stopped to transfer the patient to the ICU.

Investigational medicinal product name	PROPOFOL-LIPURO
Investigational medicinal product code	
Other name	2,6-diisopropylphenol
Pharmaceutical forms	Emulsion for emulsion for injection
Routes of administration	Intravenous use

Dosage and administration details:

The target doses are 0.5, 1, 1.5, 2 and 2.5 µg/kg. For its administration we will use the TCI (target controlled infusion) system. After programming each dose we will wait until the plasma and brain concentration of propofol are stabilized in this target and then we will record the local field potentials activity through the DBS. In addition, the subscales of rigidity, tremor and bradykinesia of the UPDRS-

III score will be evaluated.

Number of subjects in period 1	Treatment
Started	12
Completed	11
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period

Reporting group description:

A total of 12 patients with PD were invited to participate in this study. The participation rate was 100%. One patient was excluded due to an intraoperative adverse event. This patient experienced pharyngeal dystonia and developed dyspnea before DBS implantation, leading to a change in the anesthesia from cooperative sedation to general anesthesia. We also excluded from the analyses the unique patient whose target nucleus was GPi.

Reporting group values	Treatment period	Total	
Number of subjects	12	12	
Age categorical 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)	8	8	
From 65-84 years	3	3	
85 years and over	1	1	
Adults	0	0	
Gender categorical Units: Subjects			
Female	2	2	
Male	10	10	

End points

End points reporting groups

Reporting group title	Treatment

Reporting group description:

Experimental: Dexmedetomidine recording
Recording registered through the deep brain stimulation electrodes with dexmedetomidine at 0.2 µg/kg/h.
Intervention: Drug: Dexmedetomidine

Active Comparator: Propofol recording
Recording registered through the deep brain stimulation electrodes with propofol at plasmatic levels of 0.5, 1, 1.5, 2, 2.5 µg/mL.
Intervention: Drug: Propofol

No Intervention: Basal recording
Recording registered through the deep brain stimulation electrodes with no sedation .

Primary: Changes in LFP recordings. Propofol

End point title	Changes in LFP recordings. Propofol[1]

End point description:

Study whether there are changes (and their characteristics) in local field potentials recordings in deep subcortical structures, obtained through the stimulators implanted to treat Parkinson's disease, with the administration of dexmedetomidine and propofol. Data are shown as the mean difference between baseline and prpofol LFP . There was a significant decline of 12.7% (95% CI, −21.3 to −4.7) in the relative beta power of the local field potentials for each increment in the estimated peak propofol concentrations at the effect site relative to the control recordings.

End point type	Primary

End point timeframe:

Propofol was administered (about 2 hours) one day after the stimulator reading (baseline).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A significant 12.7% (95% CI, 4.1 to 21.3) decline in the LFPs relative to the control recordings was evident for eachincrement in the estimated peak effect site concentration of propofol (0.5, 1.0, 1.5, 2.0, and 2.5 µg/ml) when all nuclei were analyzed.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: p value				
number (not applicable)				
p value	0.004			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in LFP recordings. Dexmedetomidine

End point title	Changes in LFP recordings. Dexmedetomidine[2]

End point description:

End point type	Primary

End point timeframe:

Dexmedetomidine was administered (for about 6 hours), 3-4 days before the stimulator readind.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Dexmedetomidine administration at 0.2 µg·kg-1·h-1 caused minimal changes in the power distribution. Accordingly, no significant difference was observed when comparing the relative beta power of LFPs (RBP-LFPs) between dexmedetomidine and control recordings, with a mean difference in the RBP-LFPs between dexmedetomidine and control recordings of −7.7 (95% CI, −18.9 to 3.8) when all nuclei were analyzed.

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: p value				
number (not applicable)	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In the event that an SAE occurs, it must be notified within 24 hours after having knowledge of the event. Any SAE that occur after the completion of the trial should be reported if the investigator believes the SAE is related to the study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	ND
Dictionary version	ND

Reporting groups

Reporting group title	Experimental group

Reporting group description: -

Serious adverse events	Experimental group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Pharyngeal dyskinesias			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Vascular disorders			
Brain pressure without headache			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hematoma			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Surgical and medical procedures			

Surgical wound pain subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 6		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Tremor in ESI subjects affected / exposed occurrences (all) Drowsiness subjects affected / exposed occurrences (all) Motor block sensation subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Vasovagal reaction subjects affected / exposed occurrences (all)	 5 / 12 (41.67%) 5 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2 5 / 12 (41.67%) 5 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Blood and lymphatic system disorders Leukocytosis subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
General disorders and administration site conditions Malaise subjects affected / exposed occurrences (all) Loss of appetite subjects affected / exposed occurrences (all)	 5 / 12 (41.67%) 5 1 / 12 (8.33%) 1		
Immune system disorders Sickness			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Apathy subjects affected / exposed occurrences (all) Anxiety disorder subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 3 / 12 (25.00%) 3 2 / 12 (16.67%) 2		
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Shoulder pain subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Gout subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 2 / 12 (16.67%) 2 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		

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