Clinical trial results:
The Efficacy of Ibogaine in the Treatment of Addiction; an open label, single fixed dose pilot-study of the efficacy of ibogaine in opioid-dependent subjects

Summary

EudraCT number	2014-000354-11
Trial protocol	NL
Global end of trial date	30 October 2019

Results information

Result version number	v1
This version publication date	07 May 2022
First version publication date	07 May 2022
Summary attachment (see zip file)	Safety of ibogaine administration~1 Knuijver et.al. (Addiction - 2021 - Knuijver - Safety of ibogaine administration in detoxification of opioiddependent individuals a.pdf)

Trial information

Trial identification

Sponsor protocol code	ABR47613

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dept Psychiatry, Radboucumc, Nijmegen
Sponsor organisation address	Reinier Postlaan 10, Nijmegen, Netherlands, 6525 GC
Public contact	Dept Psychiatry 966, Radboud UMC, 31 243613490, robbert-jan.verkes@radboudumc.nl
Scientific contact	Dept Psychiatry 966, Dept Psychiatry, Radboudumc, 31 243613490, robbert-jan.verkes@radboudumc.nl

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	30 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2018
Global end of trial reached?	Yes
Global end of trial date	30 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To investigate, in patients with opioid dependence, the short and long term effects of a single administration of ibogaine on cardiac, cerebellar and psychomimetic safety, craving and substance use during immediately after detoxificationa and during a six month follow up period.

Protection of trial subjects:

During the 24 hours after administration of the drug, participants are in calm, single hospital room with a bed and with continuous monitoring.
Electrocardiographic monitoring (ECG) is performed every half hour for the first 12 hours. Thereafter, ECG measurements will be performed every hour in case of persistent QTc prolongation (> 450 ms for men; > 470 ms for women) or every 4 hours if automatic QTc time is shortening and below 500 ms. ECG measurements will be continued for 24 hours after administration. After 24 hours a cardiologist will assess the ECG if monitoring needed to continue. If, after administration of the ibogaine, QTc exceeds 500 ms, participants will receive a magnesium bolus infusion of 2 g in 10minutes, followed by 2 g of magnesium over the next 10 hours for myocardial stabilization. If necessary, subjects can be transferred to the coronary care unit (CCU) for continuous cardiac monitoring.
Symptoms of ataxia, delirium, and withdrawal symptoms will be monitored and scored 1,6,10 and 24 hours after drug administration.

Background therapy:

Before ibogaine administration subjects will be given 20 mg of metoclopramide to prevent nausea for comfort and to ensure full ingestion.

Evidence for comparator:

not applicable

Actual start date of recruitment	01 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at two outpatient addiction clinics (IrisZorg: Arnhem and Nijmegen). 36 patients deemed eligible were approached to participate; 29 patients were willing and were screened, 14 actually participated. Inclusion took place between October 2015 and November 2017.

Pre-assignment

Screening details:

Inclusion criteria: 20–60 yrs of age, a wish for detoxification of opioids and prior treatment failure. Exclusion criteria: a history of clinically significant cardiac disease, serum potassium > 5.0 or < 3.5 mmol/l, severe liver or renal dysfunction or pregnancy, (a history of) psychotic symptoms, severe major depressive disorder or suicidality.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

not blinded

Arms

Arm title	study cohort

Arm description:

There is only one arm

Arm type	Experimental
Investigational medicinal product name	ibogaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

ibogaine-HCl 10mg/kg orally administered in a yoghurt mixture

Number of subjects in period 1	study cohort
Started	14
Completed	14

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description:

14 subjects entered the study, 12 men, 2 women.
Besides opioids there was other drug use 1 month prior to detoxification:
Alcohol 2/14
Amphetamine 0/14
Benzodiazepines 3/14
Cannabis 4/14
Cocaine 7/14
Heroin 8/14
Tobacco 13/14

Reporting group values	overall trial	Total	
Number of subjects	14	14	
Age categorical			
Age (median; 25th and 75th percentile) 48 (44–51)			
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)	14	14	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
median: 48 ; 25th and 75th percentile: 44–51			
Units: years			
median	48		
inter-quartile range (Q1-Q3)	44 to 51	-	
Gender categorical			
12 men, 2 women			
Units: Subjects			
Female	2	2	
Male	12	12	

End points

End points reporting groups

Reporting group title	study cohort
Reporting group description:	
There is only one arm	
Subject analysis set title	baseline data
Subject analysis set type	Safety analysis
Subject analysis set description:	
Baseline QTc	
Subject analysis set title	QTc after administration
Subject analysis set type	Safety analysis
Subject analysis set description:	
All QTc measurements of the 24 hour period after ibogaine administration	

Primary: difference between the QTc (ECG) before administration and the maximum QTc during the observation period

End point title	difference between the QTc (ECG) before administration and the maximum QTc during the observation period[1]
End point description:	
End point type	Primary
End point timeframe:	
until 24 hoursafter drug administration	

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: SD Mean and range of ΔQTcMax are discriptive statistics. There was no p-value calculated.

End point values	study cohort			
Subject group type	Reporting group			
Number of subjects analysed	14[2]			
Units: msec				
median (standard deviation)	102 (± 40)			

Notes:

[2] - all sujects were abalyzed

Statistical analyses

No statistical analyses for this end point

Secondary: SARA

End point title	SARA
End point description:	
Measurement of the severity of ataxia	
End point type	Secondary
End point timeframe:	
During the first 24 hours (0, 2, 6, 10 and 24)	

End point values	study cohort			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Score				
number (not applicable)	14			

Statistical analyses

No statistical analyses for this end point

Secondary: DOS

End point title	DOS
End point description: Delerium observation scale	
End point type	Secondary
End point timeframe: 24 hours after administration	

End point values	study cohort			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Score				
number (not applicable)	14			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First 24 hours after drug administration

Adverse event reporting additional description:

ECGs every half hour for the first 12 hours, then the second 12 hours every hour in case of persistent QTc prolongation
or every 4 hours if automatic QTc time was shortening and below
500 ms.
Ataxia and and psychomimetic (delirium) were assessed at 2, 6, 10 and
24 hours after administration of ibogaine.

Assessment type	Systematic

Dictionary used

Dictionary name	no dictionary used
Dictionary version	0

Reporting groups

Reporting group title	study sample

Reporting group description:

study sample

Serious adverse events	study sample		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	study sample		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 14 (50.00%)		
Cardiac disorders			
prolonged QTc time	Additional description: Half the participants reached a QTc of >500 msec ECG abnormalities, including QTc > 450 ms for men and > 470 ms for women, were reason for exclusion to enter the trial.		
subjects affected / exposed	7 / 14 (50.00%)		
occurrences (all)	7		
Nervous system disorders			
Ataxia	Additional description: All subjects developed clinical signs of cerebellar ataxia, with full remission within 24 hours after ibogaine administration.		

subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	1		
Psychomimetic effects	Additional description: In two subjects delirious signs were observed, in full remission after 24 hours		
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2014	Due to financial constraints, fMRI research was dropped from this protocol
15 June 2016	On the 15th of June a request was made to allow a 61-year old subject to enter the study
14 December 2016	Intent to increase from 12 to 15 subjects (14 were eventually inlcuded) Ibogaine INIRI monitorrapport 2 2016-12-14_draft1
06 May 2019	Retrospective monitoring report, these are minor adjustments made to accomodate the intent of measuring depression, ataxia and delerium, aswell as bloodwithdrawals. - Addition of: Becks Depression Inventory, SARA, SOWS and OOWS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33620733