Clinical trial results:
Botulinumtoxin A for emotional stabilization in borderline personality disorder

Summary

EudraCT number	2015-000749-21
Trial protocol	DE
Global end of trial date	10 May 2019

Results information

Result version number	v1 (current)
This version publication date	03 January 2024
First version publication date	03 January 2024

Trial information

Trial identification

Sponsor protocol code	BOTOX III

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02728778
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	31 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2019
Global end of trial reached?	Yes
Global end of trial date	10 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigation of glabellar injections of Botulinumtoxin A in treatment of borderline personality disorder

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2016
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	Germany: 53
Worldwide total number of subjects	53
EEA total number of subjects	53

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)	53
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient/trial person diagnosed with borderline personality disorder (ICD 10: F60.31)

Pre-assignment

Screening details:

Eligibility will be determined based upon the inclusion and exclusion criteria.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

There is a blinded and an unblinded team at each study center. The unblinded team does the injections and the unblinded team is responsible for the psychometrical rating.
participants are not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Acupuncture

Arm description:

Four treatments of acupuncture at intervals of 2 weeks.

Arm type	acupuncture control group

No investigational medicinal product assigned in this arm

Arm title	Botulinum toxin

Arm description:

Single intramuscular injection of Bocouture®-solution at five sites of Mm. corrugatores supercilii et procerus with a sterile 0.3 ml insulin syringe (30 gauge)

Arm type	Experimental
Investigational medicinal product name	Botulinumtoxin A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single intramuscular injection of Bocouture®-solution at five sites of Mm. corrugatores supercilii et procerus with a sterile 0.3 ml insulin syringe (30 gauge)

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Blinding is only single blind and the psychometrical rating was done by a blinded assessor team

Number of subjects in period 1	Acupuncture	Botulinum toxin
Started	26	27
Completed	19	23
Not completed	7	4
Hospitalization	1	-

Discontinued	5	-
Lost to follow-up	-	4
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Acupuncture
Reporting group description:	
Four treatments of acupuncture at intervals of 2 weeks.	
Reporting group title	Botulinum toxin
Reporting group description:	
Single intramuscular injection of Bocouture®-solution at five sites of Mm. corrugatores supercilii et procerus with a sterile 0.3 ml insulin syringe (30 gauge)	

Reporting group values	Acupuncture	Botulinum toxin	Total
Number of subjects	26	27	53
Age categorical			
Participants with diagnosed BPD; female sex, age 18–40 years, stable treatment for at least 8 weeks prior to and after enrollment			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	27.96	30.44	
standard deviation	± 5.74	± 5.80	-
Gender categorical			
Units: Subjects			
Female	26	27	53
Male	0	0	0

End points

End points reporting groups

Reporting group title	Acupuncture
Reporting group description:	
Four treatments of acupuncture at intervals of 2 weeks.	
Reporting group title	Botulinum toxin
Reporting group description:	
Single intramuscular injection of Bocouture®-solution at five sites of Mm. corrugatores supercilii et procerus with a sterile 0.3 ml insulin syringe (30 gauge)	

Primary: Increase in ZAN-BPS values

End point title	Increase in ZAN-BPS values
End point description:	
The primary efficacy endpoint is the relative increase in ZAN-BPS values from week 8 to baseline, compared between the treatment groups (BTX treatment versus ACU control) and adjusted for centers (Hamburg versus Hannover). As defined in the protocol the relative difference between ZAN-BPS scores at baseline za0 and at week 8 za8 is compared between the treatment groups. The null hypothesis of no difference between the groups is examined.	
End point type	Primary
End point timeframe:	
visits occur at week 2, 4, 6, 8, 12 and 16	

End point values	Acupuncture	Botulinum toxin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: : Differences in mean values of ZAN-BPS				
arithmetic mean (standard deviation)	-0.346 (± 0.418)	-0.388 (± 0.389)		

Statistical analyses

Statistical analysis title	equality of treatment means
Statistical analysis description:	
ANOVA Table (type II test): increase in ZAN-BPS between treatment	
Comparison groups	Acupuncture v Botulinum toxin

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.68
Method	ANOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Der Dokumentationszeitraum für diese Klinische Prüfung beginnt mit der einmaligen Verabreichung des Prüfpräparates und endet mit der letzten Visite (16 Wochen nach Verabreichung).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Acupuncture
Reporting group description: -	
Reporting group title	Botulinumtoxin A

Reporting group description: -

Serious adverse events	Acupuncture	Botulinumtoxin A	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 26 (7.69%)	4 / 27 (14.81%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Cholezystektomie			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Borderline Persoenlichkeitsstoerung			
subjects affected / exposed	2 / 26 (7.69%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suizidgedanken			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			

subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Acupuncture	Botulinumtoxin A	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 26 (38.46%)	15 / 27 (55.56%)	
Injury, poisoning and procedural complications			
Absichtliche Ueberdosis			
subjects affected / exposed	0 / 26 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	3	
Bandruptur			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Kontusion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Kopfschmerz im Zusammenhang mit einem Verfahren			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Cardiac disorders			
Arrhythmie			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Nervous system disorders			
Kopfschmerzen			
subjects affected / exposed	4 / 26 (15.38%)	5 / 27 (18.52%)	
occurrences (all)	5	9	
Migraene			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Schwindelgefuehl			

subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Sprachstoerung			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Akne an der Applikationsstelle			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Ermuedung			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Schmerzen an der Injektionsstelle			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nichtinfektioese Gingivitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis allergisch			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Lichtempfindlichkeitsreaktion			
subjects affected / exposed	0 / 26 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Psychiatric disorders			
Absichtliche Selbstverstuemmelung			
subjects affected / exposed	0 / 26 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	4	
Einschlafstoerung			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Schlafstoerung			
subjects affected / exposed	1 / 26 (3.85%)	1 / 27 (3.70%)	
occurrences (all)	1	1	

Trauerreaktion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgie			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Genitaler Herpes			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 26 (3.85%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Otitis externa			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35102782