Clinical trial results:
Short-term efficacy of a single ultrasound-guided intra-articular injection of botulinum toxin A associated with splinting for base-of-thumb osteoarthritis on pain at 3 months: A randomized placebo-controlled pilot study

Summary

EudraCT number	2016-003939-38
Trial protocol	FR
Global end of trial date	23 April 2021

Results information

Result version number	v1 (current)
This version publication date	19 June 2022
First version publication date	19 June 2022

Trial information

Trial identification

Sponsor protocol code	P160404J

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03187626
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS (AP-HP)
Sponsor organisation address	DRCI Hôpital Saint-Louis, 1 avenue Claude Vellefaux, PARIS, France, 75010
Public contact	DRCI Hôpital St Louis, ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS (AP-HP), josephine.braun@aphp.fr
Scientific contact	AP-HP Hôpital Cochin, ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS (AP-HP), christelle.nguyen2@aphp.fr

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	12 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2021
Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy on pain at 3 months of a single ultrasound-guided intra-articular injection of (botulinum toxin A) BTA associated with splinting to a single ultrasound-guided intra-articular injection of saline associated with splinting in patients with painful Base-of-thumb osteoarthritis (BTOA)

Protection of trial subjects:

Patients benefit from specific medical monitoring and the single trapezio-metacarpal intra-articular infiltration, i.e. at the base of the thumb, is performed under ultrasound by an experienced radiologist. AP-HP has taken all measures to conduct this research in accordance with the provisions of the Public Health Code applicable to research involving humans.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 November 2018
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	France: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	34
From 65 to 84 years	24
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants to be recruited among patients seen in hospital consultation and rehabilitation hospitalization at Cochin Hospital and presenting with rhizarthrosis as well as among the patients of the DIGICODE digital osteoarthritis cohort (Hôpital Saint-Antoine) and the employees of the AP-HP via the intranet and the AP mailing list -HP

Pre-assignment

Screening details:

Participants will be recruited from outpatients and those seen in hospital consultations, occupational therapy consultations, or full or partial hospitalization in physical medicine and rehabilitation (PMR) at Hôpital Cochin with rhizarthrosis

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	botulinum toxin

Arm description:

Experimental

Arm type	Experimental
Investigational medicinal product name	toxine botulinique de type A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

50 units, administered in a single intra-articular, trapezoidal-metacarpal, ultrasound-guided injection performed by an experienced radiologist

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

1 ml NaCl 0,9%, administered in a single intra-articular, trapezoidal-metacarpal, ultrasound-guided injection performed by an experienced radiologist

Number of subjects in period 1	botulinum toxin	Placebo
Started	30	30
Completed	30	30

Baseline characteristics

Reporting groups	
Reporting group title	botulinum toxin
Reporting group description: Experimental	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	botulinum toxin	Placebo	Total
Number of subjects	30	30	60
Age categorical 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	65.2	64.6	
standard deviation	± 8.2	± 10.4	-
Gender categorical Units: Subjects			
Female	25	22	47
Male	5	8	13

End points

End points reporting groups

Reporting group title	botulinum toxin
Reporting group description: Experimental	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	intent to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: intent to treat	

Primary: Change in base of thumb pain score at 3 monts

End point title	Change in base of thumb pain score at 3 monts
End point description:	
End point type	Primary
End point timeframe: 3 months	

End point values	botulinum toxin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: number from 0 to 100				
arithmetic mean (confidence interval 95%)	-25.7 (-35.5 to -15.8)	-9.7 (-17.1 to -2.2)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	botulinum toxin v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [1]
Method	Constrained longitudinal data analysis

Notes:

[1] - p<0.05
Constrained longitudinal data analysis
Chi-squared test
Fisher's exact test

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24
Reporting groups	
Reporting group title	experimental
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Serious adverse events	experimental	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	experimental	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	24 / 30 (80.00%)	
Vascular disorders			
Localised bleeding	Additional description: bleeding		
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Thenar muscle motor deficit	Additional description: Motor dysfonction		
subjects affected / exposed	14 / 30 (46.67%)	2 / 30 (6.67%)	
occurrences (all)	14	2	
Thumb paraesthesia	Additional description: paresthesia of fingers		

subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Base-of-thumb pain	Additional description: Pain in thumb		
subjects affected / exposed	6 / 30 (20.00%)	11 / 30 (36.67%)	
occurrences (all)	6	11	
Other musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	5 / 30 (16.67%)	6 / 30 (20.00%)	
occurrences (all)	5	6	
Infections and infestations			
Intercurrent infection	Additional description: Infection NOS		
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2018	Modification of the data collection at 1 month in the protocol and in the information note: patients will complete the information concerning health status and medication consumption and the pain scale at the +1 month visit
26 June 2018	- clarification of non-inclusion criteria to "Neurological conditions affecting the hand other than carpal tunnel syndrome" and "Osteoarthritis predominating at the scaphotrapezial joint on radiographs - Modification of the practical conduct of the study by grouping the inclusion visit and the infiltration visit on the same day - Correction of the type of orthesis used: The ortheses usually used for rhizarthrosis are thermoformed plastic ortheses - Modification of the practical procedure by adding the collection of AEs at M1 at the request of the ANSM - Addition of the self-questionnaire for the collection of adverse events
28 May 2019	- 6-month extension of the duration of inclusions - Compliance of the paragraphs relating to the processing of health data with the legislative and regulatory framework of the GDPR
07 February 2020	- 6-month extension of the duration of inclusions - Addition of a non-inclusion criterion: "Patient with epilepsy": in accordance with the product's SmPC - Addition of the credibility questionnaire to the follow-up at 6 months
28 July 2020	6-month extension of the duration of inclusions

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 March 2020	inclusions suspended due to the COVID-19 pandemic from 16.03.2020, resumed on 02.06.2020	02 June 2020

Notes:

Limitations and caveats

None reported