Clinical trial results:
Functional effects of botulinum toxin in the hip adductors and subsequent exercise in patients with hereditary spastic paraplegia: a pilot RCT

Summary

EudraCT number	2015-003184-11
Trial protocol	NL
Global end of trial date	19 June 2017

Results information

Result version number	v1 (current)
This version publication date	30 November 2020
First version publication date	30 November 2020
Summary attachment (see zip file)	Summary (Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	R0002820

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud university medical center
Sponsor organisation address	Reinier postlaan 4, Nijmegen, Netherlands,
Public contact	Investigator, Radboud University Medical Centre, Bas.vanLith@radboudumc.nl
Scientific contact	Investigator, Radboud University Medical Centre, Bas.vanLith@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	10 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study is to investigate whether BTX injections, injected bilaterally in the spastic adductors of patients with HSP can improve lateral stepping and gait width.

Protection of trial subjects:

The risk of participating in this study can be considered as negligible. There is a lot of knowledge about BTX-A and the rehabilitation physicians do have a lot of experience with BTX-A, even in smaller muscle groups.
Burden associated with the measurements will be limited, since measurements were non-invasive and already clinically implemented.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 September 2015
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	Netherlands: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	20
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion criteria
Pure form HSP
18 years or older
Bilateral hip adductor spasticity
Balance- and gait-related activity limitations in daily life
Able to walk >50 m
Comfortable gait velocity >0.4 m/s

Exclusion criteria:
Cognitive impairments or comorbidity affecting gait capacity.

Period 1

Period 1 title	T0
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

n.a.

Arms

Arm title	BTX-A group

Arm description:

There is one group, and its receiving BTX-A injections.

Arm type	Experimental
Investigational medicinal product name	Xeomin
Investigational medicinal product code	0259-1620
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Bilateral Xeomin injections (fixed dose of 400 U) in the hip adductors group under ultrasound guidance, using 4 injections each side: 2 injections in the m. adductor longus (2 x 50 U)and 2 injections in the m. gracilis (2 x 50 U) (solution: 100 U in 5 mlsaline 0,9%)

Number of subjects in period 1	BTX-A group
Started	25
Completed	25

Period 2

Period 2 title	T1
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	BTX-A group

Arm description:

There only was one group. It received BTX-A

Arm type	Experimental
Investigational medicinal product name	Xeomin
Investigational medicinal product code	0259-1620
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Bilateral Xeomin injections (fixed dose of 400 U) in the hip adductors group under ultrasound guidance, using 4 injections each side: 2 injections in the m. adductor longus (2 x 50 U)and 2 injections in the m. gracilis (2 x 50 U) (solution: 100 U in 5 mlsaline 0,9%)

Number of subjects in period 2[1]	BTX-A group
Started	22
Completed	22

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: During T1, 3 patients were lost. Yet, I get an error message when this is filled in.

Period 3

Period 3 title	T2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	BTX-A group

Arm description:

There was only one group.

Arm type	Experimental
Investigational medicinal product name	Xeomin
Investigational medicinal product code	0259-1620
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Bilateral Xeomin injections (fixed dose of 400 U) in the hip adductors group under ultrasound guidance, using 4 injections each side: 2 injections in the m. adductor longus (2 x 50 U)and 2 injections in the m. gracilis (2 x 50 U) (solution: 100 U in 5 mlsaline 0,9%)

Number of subjects in period 3	BTX-A group
Started	22
Completed	22

Baseline characteristics

End points

End points reporting groups	
Reporting group title	BTX-A group
Reporting group description: There is one group, and its receiving BTX-A injections.	
Reporting group title	BTX-A group
Reporting group description: There only was one group. It received BTX-A	
Reporting group title	BTX-A group
Reporting group description: There was only one group.	

Primary: Gait width	
End point title	Gait width
End point description:	
End point type	Primary
End point timeframe: T0-T1-T2	

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: centimeters				
arithmetic mean (standard deviation)	10.7 (± 5.8)	11.8 (± 6)	11.3 (± 5.7)	

Statistical analyses

Statistical analysis title	RM - ANOVA
Comparison groups	BTX-A group v BTX-A group v BTX-A group
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)

Primary: Quality of sideways reactive stepping	
End point title	Quality of sideways reactive stepping

End point description:

End point type	Primary

End point timeframe:
T0-T1-T2

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: angles				
arithmetic mean (standard deviation)	18.7 (± 4.1)	19.8 (± 3.8)	19.3 (± 4.7)	

Statistical analyses

Statistical analysis title	ANOVA
Comparison groups	BTX-A group v BTX-A group v BTX-A group
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA

Secondary: Gait width maximal speed

End point title	Gait width maximal speed

End point description:

End point type	Secondary

End point timeframe:
Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: angles				
arithmetic mean (standard deviation)	10 (± 6)	11.5 (± 6.1)	11.2 (± 5.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Gait speed comfortable

End point title	Gait speed comfortable

End point description:

End point type	Secondary

End point timeframe:
Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: meter per second				
arithmetic mean (standard deviation)	0.96 (± 0.25)	1.04 (± 0.25)	1.07 (± 0.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: maximal gait speed

End point title	maximal gait speed

End point description:

End point type	Secondary

End point timeframe:
Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: meter per second				
arithmetic mean (standard deviation)	1.31 (± 0.41)	1.33 (± 0.35)	1.36 (± 0.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Leg angle unknow direction

End point title	Leg angle unknow direction

End point description:

All outcome measure can be found in table 3 of the open access paper

End point type	Secondary

End point timeframe:

Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: Rest				
arithmetic mean (standard deviation)	19.1 (± 4.7)	19.3 (± 4.7)	19.4 (± 5.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Success rates known dir

End point title	Success rates known dir

End point description:

End point type	Secondary

End point timeframe:

Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: Percentage				
median (inter-quartile range (Q1-Q3))	70 (45 to 90)	90 (70 to 100)	90 (55 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Success rates unknown dir

End point title	Success rates unknown dir

End point description:

End point type	Secondary

End point timeframe:
Complete study

End point values	BTX-A group	BTX-A group	BTX-A group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	22	22	
Units: Percentage				
median (inter-quartile range (Q1-Q3))	25 (0 to 55)	35 (17.5 to 90)	45 (0 to 70)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: T0-T1T2	
Assessment type	Systematic
Dictionary used	
Dictionary name	n.a.
Dictionary version	1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: There weren't any adverse events.

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