



## Clinical trial results:

### Effectiveness of Botulinum Toxin Infiltration for treatment of upper limb dysfunctions after treatment for breast cancer

#### Summary

EudraCT number	2014-005114-33
Trial protocol	BE
Global end of trial date	01 January 2020

#### Results information

Result version number	v1 (current)
This version publication date	09 February 2020
First version publication date	09 February 2020
Summary attachment (see zip file)	Manuscript Botox_UL outcomes (Botox for UL dysfunctions BC_accepted.pdf) Manuscript botox_pain outcomes (Botox_pain_accepted.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	s57283
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##### Additional study identifiers

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

Notes:

##### Sponsors

Sponsor organisation name	UZ/KULeuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Nele Devoogdt, UZ Leuven, +32 16342171, an.degroef@faber.kuleuven.Be
Scientific contact	Nele Devoogdt, UZ Leuven, +32 16342171, an.degroef@faber.kuleuven.Be

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	01 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 January 2017
Global end of trial reached?	Yes
Global end of trial date	01 January 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The aim of this study is to examine the effect of Botulinum Toxine infiltration in the pectoral muscle, in combination with an individual physical therapy programme, on pain and upper limb dysfunctions in women after breast cancer

Protection of trial subjects:

All participants gave written informed consent before data collection began.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
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	Belgium: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	41
From 65 to 84 years	9
85 years and over	0

## Subject disposition

### Recruitment

#### Recruitment details:

Patients were recruited at the Multidisciplinary Breast Center and the Department of Physical Medicine and Rehabilitation of the University Hospitals in Leuven between February 2015 and July 2016.

### Pre-assignment

#### Screening details:

All referred patients (n=103) were screened, and 50 (47%) agreed to participate. The 53 nonparticipants had more pN1 and less pN2-3 tumors ( $P=.028$ ) and had less radiotherapy ( $P=.016$ ) compared with participants. Fifty patients were included in the study and were randomly assigned to an intervention group (n=25) and a control group (n=25).

### 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, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Intervention group

#### Arm description:

Patients in the intervention group received an intramuscular injection of BTX-A (100 units, Botox) in the pectoralis major muscle. Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.

Arm type	Experimental
Investigational medicinal product name	Botulinum Toxin A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Infiltration

#### Dosage and administration details:

Patients in the intervention group received an intramuscular injection of BTX-A (100 units, Botox) in the pectoralis major muscle.

<b>Arm title</b>	Control group
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#### Arm description:

Patients in the control group received a placebo infiltration consisting of 50mL of saline (Mini-Plasco 20mL NaCl 0.9%). Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.

Arm type	Placebo
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Investigational medicinal product name	Mini-Plasco 20mL NaCl 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Infiltration

Dosage and administration details:

Patients in the control group received a placebo infiltration consisting of 50mL of saline (Mini-Plasco 20mL NaCl 0.9%). Injections were evenly spread over the muscle belly, including the clavicular and sternal part.

<b>Number of subjects in period 1</b>	Intervention group	Control group
Started	25	25
Completed	25	25

## Baseline characteristics

### Reporting groups

Reporting group title	Intervention group
Reporting group description:	
Patients in the intervention group received an intramuscular injection of BTX-A (100 units, Botox) in the pectoralis major muscle. Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.	
Reporting group title	Control group
Reporting group description:	
Patients in the control group received a placebo infiltration consisting of 50mL of saline (Mini-Plasco 20mL NaCl 0.9%). Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.	

Reporting group values	Intervention group	Control group	Total
Number of subjects	25	25	50
Age categorical			
Units: Subjects			
Adults (18-64 years)	22	19	41
From 65-84 years	3	6	9
Age continuous			
Units: years			
arithmetic mean	53.4	56.6	-
standard deviation	± 10	± 10	-
Gender categorical			
Units: Subjects			
Female	25	25	50
Male	0	0	0
Type of Breast Surgery			
Units: Subjects			
Mastectomy	12	17	29
Breast Conserving Surgery	10	6	16
Mastectomy with immediate reconstruction	3	2	5
Radiotherapy			
Units: Subjects			
Radiotherapy	25	24	49
No radiotherapy	0	1	1
Chemotherapy			
Units: Subjects			
Chemotherapy	16	17	33
No chemotherapy	9	8	17
Targeted therapy			
Units: Subjects			
Targeted therapy	1	3	4
No targeted therapy	24	22	46

Endocrine therapy			
Units: Subjects			
Endocrine therapy	22	23	45
No endocrine therapy	3	2	5
Body Mass Index			
Units: kg/m <sup>2</sup>			
arithmetic mean	24.8	28.1	
standard deviation	± 3.6	± 5.0	-

## End points

### End points reporting groups

Reporting group title	Intervention group
Reporting group description: Patients in the intervention group received an intramuscular injection of BTX-A (100 units, Botox) in the pectoralis major muscle. Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.	
Reporting group title	Control group
Reporting group description: Patients in the control group received a placebo infiltration consisting of 50mL of saline (Mini-Plasco 20mL NaCl 0.9%). Within the first week after the BTX-A or saline infiltration, all participants started an individual standard physical therapy program of 12 weeks (1 session per week) at the University Hospital Leuven. The sessions were individual and lasted 30 minutes.	

### Primary: change in pain intensity at the upper limb region 3 months after baseline

End point title	change in pain intensity at the upper limb region 3 months after baseline
End point description:	
End point type	Primary
End point timeframe: change in pain intensity at the upper limb region 3 months after baseline	

End point values	Intervention group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Visual Analogue Scale	25	25		

### Statistical analyses

Statistical analysis title	multivariate linear model for repeated measurement
Statistical analysis description: Multivariate linear model for repeated (longitudinal) measurements, using an unstructured covariance matrix. The primary analysis was change in pain intensity at the upper limb region 3 months after baseline.	
Comparison groups	Intervention group v Control group

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	19
Variability estimate	Standard deviation



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

baseline until 6 months follow-up

Assessment type	Non-systematic
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### Dictionary used

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Dictionary name	SNOMED CT
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Dictionary version	3
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Frequency threshold for reporting non-serious adverse events: 5 %

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#### 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: No non-serious events happened during the trial.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29409922>