



## Clinical trial results:

### Botulinum toxin type A as treatment for chronic myogenous orofacial pain - a randomized controlled, double-blind clinical trial

#### Summary

EudraCT number	2021-002784-21
Trial protocol	SE
Global end of trial date	18 January 2024

#### Results information

Result version number	v1 (current)
This version publication date	15 December 2024
First version publication date	15 December 2024

#### Trial information

##### Trial identification

Sponsor protocol code	20210516
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Västra Götalandsregionen
Sponsor organisation address	Biskopsbogatan 27, Mölndal, Sweden, 43180
Public contact	Institute of odontology, Sahlgrenska Academy at the University of Gotheburg, +46 317860000, info@odontologi.gu.se
Scientific contact	Institute of odontology, Sahlgrenska Academy at the University of Gotheburg, +46 317860000, info@odontologi.gu.se

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	18 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2024
Global end of trial reached?	Yes
Global end of trial date	18 January 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Evaluate whether botulinum toxin A provides a significantly better pain-relieving effect for patients with orofacial myalgia compared to saline up to 6 months via evaluation of subjective perception of pain reduction and number of millimeters of pain free mouth opening.

Protection of trial subjects:

Patients were well informed verbally and in writing about possible side effects. All procedures followed good clinical standard and hygiene. Staff handling botulinumtoxin A did were educated specifically for that treatment.

Background therapy:

Patient counselling and education, tailored self-care approaches aimed at jaw relaxation and tailored physiotherapy exercises for the jaw. Biofeedback training with EMG.

Evidence for comparator: -

Actual start date of recruitment	26 August 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	71
From 65 to 84 years	1

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

72 patients were recruited between August 26th 2022 and April 30th 2023 for both study sites "Specialistkliniken för bettfysiologi Mölndal" and "Specialistkliniken för bettfysiologi Göteborg". 36 were randomized to treatment with Botulinumtoxin A and 36 to saline (placebo).

### Pre-assignment

Screening details:

Patients were age  $\geq 18$  years, diagnosis of myalgia according to the DC/TMD (22), a minimum of six months of conservative treatment consisting of at least patient counselling, physiotherapy and biofeedback relaxation training, residual pain intensity related to orofacial myalgia of at least 40mm on 0–100 mm visual analogue scale (VAS) a

### 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, Data analyst, Carer, Assessor

### Arms

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

Arm description:

Botulinum toxin A (trade name Botox Allergan) powder for solution for injection. Using 1.0ml of sterile saline solution (Natriumklorid Fresenius Kabi 9mg/ml) the botulinumtoxin A was dissolved resulting in 100U/ml.

Patients randomized to this treatment arm were injected with a total of 1ml (100U) in a total of 10 points. 2 points on each side of the temporalis muscle and 3 points to each side of the masseter muscle, using a monopolar EMG device.

Arm type	Experimental
Investigational medicinal product name	Botox
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

Botox Allergan 100U was prepared by using 1.0ml of sterile saline solution (Natrium Fresenius Kabi 9mg/ml) to dissolve the botulinumtoxin A. 0.1ml then equalled 10U. A total of 10 points were injected with 10U per point, 2 on each side of the temporalis muscle and 3 to each side of the masseter muscle using a monopolar EMG device.

<b>Arm title</b>	Placebo
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Arm description:

Natriumklorid Fresenius Kabi 9mg/ml sterile saline solution was used as placebo. Patients randomized to this treatment arm were injected with a total of 1ml in a total of 10 points. 2 points on each side of the temporalis muscle and 3 points to each side of the masseter muscle, using a monopolar EMG device.

Arm type	Placebo
Investigational medicinal product name	Natriumklorid Fresenius Kabi 9mg/ml
Investigational medicinal product code	
Other name	Saline
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1ml Natriumklorid Fresenius Kabi 9mg/ml

<b>Number of subjects in period 1</b>	Intervention	Placebo
Started	36	36
Completed	35	34
Not completed	1	2
Pregnancy	1	-
Lost to follow-up	-	1
Protocol deviation	-	1

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	72	72	
Age categorical			
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)	71	71	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	65	65	
Male	7	7	

## End points

### End points reporting groups

Reporting group title	Intervention
Reporting group description: Botulinum toxin A (trade name Botox Allergan) powder for solution for injection. Using 1.0ml of sterile saline solution (Natriumchlorid Fresenius Kabi 9mg/ml) the botulinumtoxin A was dissolved resulting in 100U/ml. Patients randomized to this treatment arm were injected with a total of 1ml (100U) in a total of 10 points. 2 points on each side of the temporalis muscle and 3 points to each side of the masseter muscle, using a monopolar EMG device.	
Reporting group title	Placebo
Reporting group description: Natriumchlorid Fresenius Kabi 9mg/ml sterile saline solution was used as placebo. Patients randomized to this treatment arm were injected with a total of 1ml in a total of 10 points. 2 points on each side of the temporalis muscle and 3 points to each side of the masseter muscle, using a monopolar EMG device.	

### Primary: VAS pain reduction between baseline and 1 month

End point title	VAS pain reduction between baseline and 1 month
End point description:	
End point type	Primary
End point timeframe: 1 month after first injection (baseline).	

End point values	Intervention	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	36		
Units: millimetre(s)				
arithmetic mean (standard deviation)	15.4 ( $\pm$ 21.1)	14.5 ( $\pm$ 19.2)		

### Statistical analyses

Statistical analysis title	t-test
Statistical analysis description: For comparison between groups t-test was used for continuous variables.	
Comparison groups	Intervention v Placebo

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.645
upper limit	4.53
Variability estimate	Standard deviation

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### Secondary: Change millimeter pain free mouth opening between baseline and 1month

End point title	Change millimeter pain free mouth opening between baseline and 1month
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and 1month after injection	

End point values	Intervention	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	36		
Units: millimetre(s)				
arithmetic mean (standard deviation)	0.139 (± 7.407)	1.06 (± 9.95)		

### Statistical analyses

No statistical analyses for this end point

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### Secondary: Evaluate if pain reduction is correlated to psychosocial factors at baseline

End point title	Evaluate if pain reduction is correlated to psychosocial factors at baseline
End point description:	
End point type	Secondary
End point timeframe:	
Collected at baseline.	



<b>End point values</b>	Intervention	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	36		
Units: categories	36	36		

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

August 26 2022 to January 18 2024

Assessment type	Systematic
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### Dictionary used

Dictionary name	SNOMED CT
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Dictionary version	20241101
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### Reporting groups

Reporting group title	Intervention
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Reporting group description:

Botulinum toxin A (trade name Botox Allergan) powder for solution for injection. Using 1.0ml of sterile saline solution (Natriumchlorid Fresenius Kabi 9mg/ml) the botulinumtoxin A was dissolved resulting in 100U/ml.

Patients randomized to this treatment arm were injected with a total of 1ml (100U) in a total of 10 points. 2 points on each side of the temporalis muscle and 3 points to each side of the masseter muscle, using a monopolar EMG device.

Serious adverse events	Intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 36 (75.00%)		
Musculoskeletal and connective tissue disorders			
Jaw Pain	Additional description: Increased jaw pain		
subjects affected / exposed	10 / 36 (27.78%)		
occurrences (all)	10		
Headache	Additional description: Increased headache		
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	7		
Weakness of jaw muscles	Additional description: Patient experience a weakening of their jaw muscles and difficulties chewing.		

subjects affected / exposed	11 / 36 (30.56%)		
occurrences (all)	11		
Difficulty opening mouth	Additional description: Patient experiences difficulty in opening their mouth.		
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	4		

## 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