Clinical trial results:
Prevention of bladder dysfunction in acute spinal cord injury

A double-blind, randomized, placebo-controlled study to explore the effect of early treatment with Onabotulinumtoxin A in patients with detrusor overactivity due to spinal cord injury

Summary

EudraCT number	2012-002211-25
Trial protocol	NO
Global end of trial date	12 March 2019

Results information

Result version number	v1 (current)
This version publication date	08 September 2021
First version publication date	08 September 2021

Trial information

Trial identification

Sponsor protocol code	bot001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01698138
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Oslo University Hospital
Sponsor organisation address	Sognsvannsveien 20, OSLO, Norway, 0372
Public contact	Dept of Urology, Reconstructive urology, Oslo University Hospital, 47 23070000, ole.jacob.nilsen@ous-hf.no
Scientific contact	Dept of Urology, Reconstructive urology, Oslo University Hospital, 47 23070000, ole.jacob.nilsen@ous-hf.no

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 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2019
Global end of trial reached?	Yes
Global end of trial date	12 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate if intravesical injection of Botox can prevent the development of bladder dysfunction after spinal cord injury

Protection of trial subjects:

The study will be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH/Good Clinical Practice and applicable regulatory requirements. Registration of patient data will be carried out in accordance with national personal data laws.
The study subjects will be recruited shortly after a serious injury. Timing of information is very difficult in this category of patients, and must take into account the subject´s ability to process and cope with all the possible complications of their injury. Even though the prognosis is usually known two weeks post injury, many patients and relatives have still not been informed about all aspects of the injury. Obtaining informed consent without adequate information is unethical. However, giving information too early may provoke depression and other psychological reactions. Consequently, we will approach the study subject with care, and only provide detailed information about the study if we consider the subjects to be able to cope with the information. Studies have previously been conducted in this group of patients (6).
The study will involve intradetrusor injections of Onabotulinumtoxin A and bladder biopsies. Intradetrusor injection of Onabotulinumtoxin A is an established treatment for NDO, with a low rate of complications and adverse events (15). Known complications to bladder biopsies are bleeding and perforation of the bladder. To avoid the risk of intraperitoneal bladder perforations, bladder biopsies will be taken from the bladder base. An experienced consultant urologist will perform the procedures. The participants will be treated as in-patients during the procedures and follow-up. These patients are routinely given anticoagulant therapy. To avoid excessive haematuria, anticoagulant therapy will be discontinued in connection with the procedures. This may increase the risk of thromboembolism.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Efficacy
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with acute spinal cord injury (above Th11) will be included within twelve weeks from the time of injury. Before randomization, the patients will be investigated with video urodynamics to make sure the bladder is atonic and in spinal shock. Patients who have developed NDO will be excluded.

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, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo injection

Arm type	Placebo
Investigational medicinal product name	NaCl 0,9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Solution for infusion

Dosage and administration details:

intradetrusor injection of 30 ml of NaCl 0.9 %

Arm title	Onabotulinumtoxin A

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Onabotulinumtoxin A
Investigational medicinal product code	
Other name	Botox
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

intradetrusor injection of 300 U Onabotulinumtoxin A (Botox®, «Allergan») in 30 ml of NaCl 0.9 %

Number of subjects in period 1	Placebo	Onabotulinumtoxin A
Started	4	5
Completed	4	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo injection	
Reporting group title	Onabotulinumtoxin A
Reporting group description: -	

Reporting group values	Placebo	Onabotulinumtoxin A	Total
Number of subjects	4	5	9
Age categorical Units: Subjects			
Adults (18-64 years)	4	5	9
Gender categorical Units: Subjects			
Female	0	0	0
Male	4	5	9

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo injection	
Reporting group title	Onabotulinumtoxin A
Reporting group description: -	

Primary: Presence of neurogenic detrusor overactivity during cystometry

End point title	Presence of neurogenic detrusor overactivity during cystometry
End point description:	
End point type	Primary
End point timeframe: 12 months	

End point values	Placebo	Onabotulinumtoxin A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: Contracts				
Contraction with amplitude over 40cm H2O	2	0		

Statistical analyses

Statistical analysis title	suissa-shuster exact unconditional test
Comparison groups	Placebo v Onabotulinumtoxin A
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	suissa-shuster exact unconditional test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The standard time period for collecting and recording AE and SAEs will begin at administration of first dose of study drug, up til 12 months follow up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Placebo Group
Reporting group description: -	
Reporting group title	Botox-treated group

Reporting group description: -

Serious adverse events	Placebo Group	Botox-treated group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	2 / 5 (40.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract infection bacterial			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo Group	Botox-treated group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 5 (100.00%)	
Injury, poisoning and procedural complications			
knee injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Urinary tract infection bacterial			
subjects affected / exposed	4 / 4 (100.00%)	5 / 5 (100.00%)	
occurrences (all)	15	16	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
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