Clinical trial results:
Pilot study to establish laboratory methods for urine Nerve Growth Factor (NGF) and immunohistochemical staining of the vanilloid receptor (TRPV1) in bladder biopsies, following open label treatment with botulinum neurotoxin type A in patients with neurogenic detrusor overactivity (NDO) and idiopathic detrusor overactivity (IDO).

Summary

EudraCT number	2010-020944-37
Trial protocol	GB
Global end of trial date	07 March 2015

Results information

Result version number	v1 (current)
This version publication date	01 December 2018
First version publication date	01 December 2018

Trial information

Trial identification

Sponsor protocol code	09/0127

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Joint Research Office
Sponsor organisation address	1st floor Maple House, London, United Kingdom, W1T7DN
Public contact	Farhat Gilani, University College London, +44 2076796469, f.gilani@ucl.ac.uk
Scientific contact	Farhat Gilani, University College London, +44 2076796469, f.gilani@ucl.ac.uk

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	07 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish laboratory methods for detecting changes degrees of bladder stimulation via nerves following treatment with BOTOX in patients with urinary urgency incontinence due either to:
-neurological disease
-or of unknown origin.

Protection of trial subjects:

Patients were all given PILs and went through an informed consent process prior to enrolment. Patient data was anonymised.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2013
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	United Kingdom: 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)	25
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Males and females aged between 18 and 75 years inclusive.
The group with NDO will be comprised exclusively of patients with multiple sclerosis who are attending the Uro-Neurology clinics.
The group of patients with IDO will be comprised of patients without neurological disease but with urodynamically proven DO (detrusor overactivity) who ar

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	25
Number of subjects completed	25

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	not applicable
Arm description: -	
Arm type	not applicable
Investigational medicinal product name	OnabotulinumtoxinA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravesical use

Dosage and administration details:

100U to idiopathic detrusor overactivity (10x1ml injections)
200U to neurogenic detrusor overactivity (20x1ml injections)

Number of subjects in period 1	not applicable
Started	25
Completed	25

Baseline characteristics

End points

End points reporting groups

Reporting group title	not applicable
Reporting group description: -	
Subject analysis set title	clinical evaluation with ICIQ-OAB, ICIQ-LUTSqol
Subject analysis set type	Full analysis
Subject analysis set description: clinical evaluation with ICIQ-OAB, ICIQ-LUTSqol, and 3-day bladder diary at baseline (Visit0), 2-weeks post BTX-A (Visit1), and at return of symptoms (Visit2)	
Subject analysis set title	urinary BDNF/Creat and NGF/Creat levels
Subject analysis set type	Full analysis
Subject analysis set description: urinary BDNF/Creat and NGF/Creat levels also correlated with the observed clinical changes from 0.28, 0.19 and 0.29 and 0.2, 0.15, to 0.17 respectively. At the same time points decreases were also seen in BDNF and NGF bladder tissue content from 16.3, 9.14 and 11.07, and 0.41, 0.26 and 0.57 pg/g respectively.	

Primary: ICIQ-OAB and ICIQ-LUTSQOL scores

End point title	ICIQ-OAB and ICIQ-LUTSQOL scores[1]
End point description: For all patients combined, across the three time points, visitO, visit1, and visit2, ICIQ-OAB scores improved at visit1 and returned to baseline by visit2, from 39.6, 13.3, and 41.3 respectively and similarly with ICIQ-LUTSqol from 193.1, 98.2 and 191.5. Similarly bladder Diary reported daily frequency episodes changed from 10.8, 6.3, 8.9, and daily urge leakage episodes changed from 6.2, 0.8, to 3 respectively over visits 1,2 and 3.	
End point type	Primary
End point timeframe: 14/2/2013 - 7/3/2015	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Details provided in endpoint description

End point values	not applicable	clinical evaluation with ICIQ-OAB, ICIQ-LUTSqol	urinary BDNF/Creat and NGF/Creat levels	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: QOL questionnaire score				
number (not applicable)	19	19	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary BDNF/Creat and NGF/Creat levels

End point title	Urinary BDNF/Creat and NGF/Creat levels
End point description: At these time points urinary BDNF/Creat and NGF/Creat levels also correlated with the observed clinical changes from 0.28, 0.19 and 0.29 and 0.2, 0.15, to 0.17 respectively. At the same time points	

decreases were also seen in BDNF and NGF bladder tissue content from 16.3, 9.14 and 11.07, and 0.41, 0.26 and 0.57 pg/g respectively.

End point type	Secondary

End point timeframe:

february 2013 - 7/3/15

End point values	not applicable	clinical evaluation with ICIQ-OAB, ICIQ-LUTSqol	urinary BDNF/Creat and NGF/Creat levels	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25			
Units: pg/g				
number (not applicable)	25	25	25	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

14/2/13-7/3/15

Adverse event reporting additional description:

2 NON SERIOUS ADVERSE EVENTS.
1 PATIENT WITH RASH - patient reported this months after treatment.
1 PATIENT WITH UTI - withdrawn from study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	Sponsors definitions
Dictionary version	1

Frequency threshold for reporting non-serious adverse events: 1 %

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 were 2 non serious AEs
One UTI and One rash post botox injection
These were both reported

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