A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Safety and Efficacy of a Single Treatment with Two Dose Levels of BOTOX?? (Botulinum Toxin Type A) Purified Neurotoxin Complex Followed by a Treatment with BOTOX?? in Patients with Urinary Incontinence Due to Neurogenic Detrusor Overactivity

Published: 19-06-2007
Last updated: 08-05-2024

Objective: The principal objective is to evaluate the safety and efficacy of two doses of BOTOX (200 Units or 300 Units) compared with placebo injected into the bladder wall in patients who have urinary incontinence due to neurogenic detrusor...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON31043

Source
ToetsingOnline

Brief title
BOTOX® in patients with Neurogenic Detrusor Overactivity

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
Detrusor Overactivity / Overactive Bladder

Research involving
Human

Sponsors and support

Primary sponsor: GCP Service bvba
Source(s) of monetary or material Support: bedrijf Allergan Inc

Intervention

Keyword: BOTOX®, Neurogenic Detrusor Overactivity, Overactive Bladder, Urinary Incontinence

Outcome measures

Primary outcome

Number of episodes of urinary incontinence as recorded by patient bladder diary

during the 7 days prior to each study visit (telephone and clinic). Primary

timepoint is at Week 6 following the first treatment

Secondary outcome

Secondary

Maximum cystometric capacity (MCC) (mL) by urodynamics as determined by the

independent central reviewer

Peak (amplitude) detrusor pressure during first involuntary detrusor

contraction (MDP) (cm H2O) by urodynamics as determined by the independent

central reviewer

Incontinence Quality of Life Instrument (I-QOL) total summary score as

completed by the patient. The I-QOL is a validated, disease-specific quality

of life questionnaire designed to measure impact of urinary incontinence on

patients* lives

Study description

Background summary

Overactive Bladder can result from neurological disease such as in patients with spinal cord injury or multiple sclerosis. This results in inappropriate and involuntary bladder contractions (called neurogenic detrusor overactivity) often leading to incontinence. These patients develop bladders that cannot hold as much urine as a healthy person. Futhermore, the pressures within the bladder are abnormally high and can lead to an increased risk of kidney damage. Botulinum neurotoxins (such as BOTOX) are known to block the release of acetylcholine (the chemical signal which triggers the bladder to contract). The toxin is locally acting and has a transient (temporary) effect. BOTOX injected into the bladder detrusor muscle has been shown to block the unwanted bladder contractions and the effect can last for many months after a treatment

Study objective

Objective: The principal objective is to evaluate the safety and efficacy of two doses of BOTOX (200 Units or 300 Units) compared with placebo injected into the bladder wall in patients who have urinary incontinence due to neurogenic detrusor overactivity. These patients will have not been adequately managed with anticholinergic drug therapy.

Study design

Study design / population
This will be a multicenter, double-blind, randomized, placebo-controlled, parallel-group study to assess the safety and efficacy of treatments with two dosages of BOTOX® in patients with neurogenic detrusor overactivity. Approximately 260 patients will be randomised at approximately 50 sites. The representative sub-groups of this population are spinal cord injury or multiple sclerosis patients with urinary incontinence who have not been adequately managed with anticholinergic therapy. Study randomization will be stratified to treatment by centre according to overactive bladder etiology (spinal cord injury or multiple sclerosis) and concurrent anticholinergic therapy at screening (use or non-use). Patients will be randomized at Day 1 to receive one of 2 doses of BOTOX® (200 U or 300 U) or placebo in a ratio of 1:1:1. Enrolment will be managed across all study centres so that approximately 50% of the patients randomized will be of spinal cord injury etiology and 50% of

multiple sclerosis etiology. Following a minimum of 12 weeks after treatment 1, patients are eligible to receive a second treatment if re-treatment criteria are met. Patients receiving BOTOX® for the first treatment will continue to be treated with the same dose received for the first treatment. Patients receiving placebo for the first treatment will receive either BOTOX® 200 U or 300 U according to a randomization schedule assigned prior to the beginning of the first treatment. Only one treatment randomization number will be assigned to each patient prior to the beginning of the first treatment, and will be associated with one of the following treatment sequences:
Treatment Sequences
1) BOTOX® 200U (treatment 1) / BOTOX® 200 U (treatment 2); 2) BOTOX® 300U (treatment 1) / BOTOX® 300 U (treatment 2); 3) Placebo (treatment 1) / BOTOX® 200 U (treatment 2); 4) Placebo (treatment 1) / BOTOX® 300 U (treatment 2)
The above treatment sequence will have a ratio of 1:1:0.5:0.5.
All patients will be followed for safety and efficacy for 104 weeks from Randomization/Day 1 or for 12 weeks following treatment 2, whichever occurs sooner.

Intervention

The studymedication is injected in the bladder wall through cystoscopy administered as 30 mL injections each of 1 mL, evenly distributed into the detrusor, avoiding the trigone and base.

Study burden and risks

see section E

Contacts

Public
GCP Service bvba

Plein 35
9970 Kaprijke
Nederland
Scientific
GCP Service bvba

Plein 35
9970 Kaprijke
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

[1] Patient is male or female, aged 18 to 80 years old [2] Patient weighs * 50 kg (110 lb) [3] Written informed consent has been obtained [4] Written Authorization for Use and Release of Health and Research Study Information (US sites only) has been obtained [5] Written Data Protection Consent (European sites only) has been obtained [6] Written documentation has been obtained in accordance with the relevant country and local privacy requirements, where applicable [7] Patient has urinary incontinence as a result of neurogenic detrusor overactivity for a period of at least 3 months prior to screening as a result of spinal cord injury or multiple sclerosis, determined by documented patient history. In addition [7a] Spinal cord injury patients must have a stable neurological injury level at T1 or below (cervical injuries are excluded) occurring * 6 months prior to screening; [7b] Multiple sclerosis patients must be clinically stable in the investigator*s opinion, for * 3 months prior to screening and have an Expanded Disability Status Scale (EDSS) score * 6.5. [8] Patient has detrusor overactivity (defined as a phasic rise in bladder pressure during the filling phase determined by urodynamics) demonstrated during the screening period or Day 1 (prior to randomization) [9] Patient is able to complete study requirements including electronic bladder diary completion and attend all study visits (telephone and clinic), in the opinion of the investigator [10] Patient has not been adequately managed with one or more anticholinergics for their urinary incontinence, in the opinion of the investigator. Not adequately managed is defined as an inadequate response or intolerable side effects after at least one month of anticholinergic therapy on an optimized dose [11] For patients taking anticholinergic medication for their neurogenic overactive bladder, dose is stable and patient is willing to maintain same dosing during study participation [12] Patient has a negative pregnancy result if female and of childbearing potential The following criteria are also required for entry into the study at Randomization/Day 1: [13] Patient experiences * 14 episodes of urinary incontinence per week with no more than 2 incontinent-free days, determined by completion of patient bladder diary during the screening period [14] Patient currently uses or is willing to use clean intermittent catheterization (CIC) to empty the bladder (indwelling catheter is not permitted). Patients currently on CIC should be willing to maintain an established CIC frequency

throughout the study. Caregiver may perform CIC [15] Patients with a negative urine culture result must take an antibiotic medication for 3 days immediately prior to Randomization/Day 1 and agree to continue antibiotic medication for at least 3 days following treatment. Patients with a positive urine culture result indicating urinary tract infection (UTI), must take an antibiotic to which the identified organism is sensitive for at least 5 days immediately prior to Randomization/Day 1 and continue for 3 days following the procedure (or longer as needed) and patient is asymptomatic for UTI on day of treatment. A UTI is defined as either a positive urine culture result with a bacteriuria count of > 10^5 CFU/mL conjoint with a leukocyturia > 5/hpf at screening or a positive urine culture that, in the investigator*s opinion, requires antibiotic therapy

Exclusion criteria

1] Patient has history or evidence of any pelvic or urological abnormalities including but not limited to the following: [1a] elevated serum creatinine > 2 times the upper limit of normal (reference range) [1b] history of or current hematuria, [1ba] if the hematuria is determined to be due to a pathologic condition or [1bb] is uninvestigated [1c] interstitial cystitis in the opinion of the investigator [1d] bladder stones within 6 months of screening [1e] surgery or bladder disease other than detrusor overactivity that may impact bladder function with the exception of surgeries for bladder stones (> 6 months) and stress incontinence, uterine prolapse, rectocele, or cystocele (>1 year) from screening [2] Patient has had previous or current botulinum toxin therapy of any serotype for any urological condition or, treatment within 3 months of Randomization/Day 1 for any other condition or use. [3] Patient has been immunized for any botulinum toxin serotype. [4] Patient discontinued anticholinergic medication for overactive bladder < 21 days prior to Randomization/Day 1. [5] Patient has a history or current diagnosis of bladder cancer or has urine cytology results which may indicate bladder cancer not ruled out by investigator at Randomization/Day 1. Suspicious urine cytology abnormalities require the investigator*s assessment to ensure that the findings are not indicative of malignancy. [6] Patient is male with previous or current diagnosis of prostate cancer. Patients with a PSA level greater than 4.0 ng/mL will require a biopsy to rule out prostate cancer, unless a prostatic biopsy has been performed on the patient within the past 12 months. [7] Patient has a detrusor compliance below 20 mL/cm H_2O by urodynamic evaluation performed during the screening period through Day 1 (prior to randomization). [8] Patient has 24 hour total volume voided > 3000 mL of urine determined by completion of patient bladder diary collected over one consecutive 24 hour period during the 7 day diary collection period prior to Randomization/Day1. [9] Patient has a post void residual volume above 150 mL for patients who micturate or have a mixed catheterization/micturition pattern. [10] Patient has an active genital infection, other than genital warts, either concurrently or within 4 weeks prior to screening. [11] Patient uses any anti-platelet or anticoagulant therapy or is using medications with anticoagulative effects within 3 days prior to treatment. Some medications may need to be withheld for > 3 days per clinical judgment of the investigator. [12] Patient has hemophilia or other clotting factor deficiencies or disorders that cause bleeding diatheses. [13] Patient has had concurrent treatment or treatment within 6 months of Randomization/Day 1 with capsaicin or resiniferatoxin. [14] Patient is currently using or plans to use an implanted or non-

implantable electrostimulation/neuromodulation device for treatment of overactive bladder. [15] Patient has a known allergy or sensitivity to any components of the study medication, anesthetics or antibiotics or any other products associated with the treatment and general study procedures. [16] Patient has any medical condition that may put the patient at increased risk with exposure to BOTOX® including diagnosed myasthenia gravis, Eaton-Lambert syndrome or amyotrophic lateral sclerosis. [17] Patient is female and pregnant, nursing or planning a pregnancy during the study, or of childbearing potential and unable or unwilling to use a reliable form of contraception during the study. [18] Patient is currently or has previously participated in another therapeutic or device study within 30 days of screening. [19] Patient has any condition or situation which, in the investigator*s opinion, puts the patient at significant risk, could confound the study results, or may interfere significantly with the patient*s participation in the study

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-10-2007
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BOTOX
Generic name:	Botulinum Toxin Type A
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-06-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-000192-42-NL
CCMO	NL16897.029.07