A Multicenter, Long-term Follow-up Study of the Safety and Efficacy of BOTOX® (Botulinum Toxin Type A) Purified Neurotoxin Complex in Patients with Urinary Incontinence Due to Neurogenic Detrusor Overactivity

Published: 28-04-2009
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Objective: The principal objective is To evaluate the long-term safety and maintenance of efficacy of BOTOX® (200 U) injected into the detrusor for the treatment of urinary incontinence caused by neurogenic detrusor overactivity in patients who have...

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

Summary

ID

NL-OMON37968

Source
ToetsingOnline

Brief title
BOTOX® in patients with Neurogenic Detrusor Overactivity / Botox 094

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
Detrusor Overactivity / Overactive Bladder

Research involving

Human

Sponsors and support

Primary sponsor: Allergan Ltd.
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 3 consecutive days prior to each study visit. The change from baseline in the daily average frequency of episodes of urinary incontinence.

The primary efficacy time point is Week 6 after each treatment in this study.

Secondary outcome

* 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

* Time between treatments

* Total volume voided recorded over one 24-hour period as recorded by patient bladder diary for all voids (catheterization and voluntary)

* Number of episodes of voiding and method (catheterization and voluntary) as recorded by patient bladder diary

In addition, urodynamic assessments will be performed at sites that agree to

perform urodynamics and for those patients who agree to undergo the procedure

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 long-term safety and maintenance of efficacy of BOTOX® (200 U) injected into the detrusor for the treatment of urinary incontinence caused by neurogenic detrusor overactivity in patients who have not been adequately managed with anticholinergic therapy.

Study design

Study design / population
This will be a multinational, multicenter, long-term follow-up study. Patients will participate in the study for up to 156 weeks (3 years) following Study Entry/Day1. Patients from study 191622-515 or 191622-516 who have completed at least 52 weeks of study participation, with at least 12 weeks of follow-up post treatment after the most recent treatment or completed the applicable Week 12/Exit visit after the last treatment, can be enrolled. Patients enter this long-term study after successful completion of the preceding study. Once treatment criteria have been met, all patients will receive active treatment in the 191622-094 study, at the dose level (BOTOX® 200 U).
Study treatment can continue to be administered up to week 144 from entry into the study.

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
Allergan Ltd.

Marlow International, The Parkway 1
Marlow, Buckinghamshire SL7 1YL
GB
Scientific
Allergan Ltd.

Marlow International, The Parkway 1
Marlow, Buckinghamshire SL7 1YL
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patient has successfully completed participation in study 191622-515 or 191622-516 and the following criteria are fulfilled:
* Patient has completed at least 52 weeks in the preceding study, with at least 12 weeks of follow-up after the last treatment, ie, has:

o completed the applicable Week 52 Exit visit or
o completed the applicable Week 12/Exit visit after the last treatment
* No longer than 6 months has elapsed since completion of the preceding study
2. Written informed consent has been obtained.
3. Written Data Protection Consent has been obtained.
4. Written documentation has been obtained in accordance with the relevant country and local privacy requirements, where applicable.
5. Patient is able to complete study requirements including diary completion and attend all study visits, in the opinion of the investigator.
6. Patient currently uses or is willing to use clean intermittent catheterization (CIC) to empty the bladder (indwelling catheter is not permitted). Caregiver may perform CIC.
7. Patient has a negative pregnancy result if female and of childbearing potential.
8. Patient weighs more than or equal to 50 kg (110 lb). Additionally, for the patient to qualify for treatment, the following criteria must be satisfied (the request for treatment can occur either at a scheduled visit or between scheduled visits): * Patient must initiate request for treatment
9. Patient reports at least 1 urinary incontinence episode in 3 days as determined by completion of patient bladder diary (over 3 consecutive days) prior to visit.
10. A minimum of 12 weeks must have elapsed since previous study treatment (either in the preceding study or in the current study) and treatment cannot occur later than 144 weeks from Study Entry/Day 1
11. A minimum of 12 weeks must have elapsed since any BOTOX® (botulinum toxin type A) treatment for any non-urological condition (use of any botulinum toxin of any serotype, is prohibited for the treatment of urological conditions, except for treatment administered as part of study participation) Once the above criteria have been met, the patient will be considered qualified for treatment. ;The following criteria must be met prior to the patient being treated with study medication:
12.Investigator determines treatment appropriate and no condition or situation exists which, in the investigator*s opinion, puts the patient at significant risk from treatment
13. Patient has discontinued any antiplatelet or anticoagulant therapy or medications with anticoagulative effects within at least 3 days prior to treatment (some medications may need to be withheld for >3 days per clinical judgment of the investigator). If needed, low molecular weight heparin can be given up to 24 hours prior to treatment
14. Negative pregnancy test result for women of childbearing potential
15 In the investigator*s opinion, patient is asymptomatic for urinary tract infection (UTI) on day of treatment
16. Patient has taken appropriate antibiotic medication:
a) For patients with a negative urine culture result, an antibiotic must be taken for at least 3 days immediately prior to study treatment and continued for at least 3 days following the study treatment procedure (or longer as needed)
b) For patients with a positive urine culture (defined as a urine culture result with a bacteriuria count of > 105 CFU/mL), an antibiotic to which the identified organism is sensitive must be taken at least 5 days immediately prior to study treatment and continued for 3 days following the study treatment procedure (or longer as needed)
17 No occurrence of bladder stones
18 For male patients at treatment one only: if PSA results are * 4.0 ng/mL and * 10.0 ng/mL, prostate cancer must be ruled out to the satisfaction of the investigator according to local

site practice prior to treatment. If the PSA is greater than 10.0 ng/mL, the patient must be discontinued from the study

Exclusion criteria

1. Patient has evidence of any pelvic or urological abnormalities including but not limited to the following: * interstitial cystitis in the opinion of the investigator
* presence of bladder stones, including any bladder stones detected in the previous study
* surgery or bladder disease other than detrusor overactivity that may impact bladder function (with the exception of surgery performed more than 1 year from screening in the preceding study for stress incontinence, uterine prolapse, rectocele, or cystocele)
2. Patient has received botulinum toxin therapy of any serotype for any urological condition (except for treatment administered as part of study participation in the preceding protocol).
3. Patient has had treatment within 12 weeks of Study Entry/Day 1 of botulinum toxin of any serotype for any non-urological condition
4. Patient has been immunized for any botulinum toxin serotype.
5. Patient has a history, or current diagnosis of prostate cancer.
6. Patient has a history, or current diagnosis of bladder cancer.
7. Patient has hemophilia or other clotting factor deficiencies or disorders that cause bleeding diatheses.
8. Patient has concurrent treatment or treatment within 6 months of Study Entry/Day 1 with intravesical capsaicin, resiniferatoxin, or any other intravesical treatment for overactive bladder.
9. Patient is currently using or plans to use an implanted or non-implantable electrostimulation/neuromodulation device for the treatment of overactive bladder or a baclofen pump.
10. Patient has a known allergy or sensitivity to any botulinum toxin preparation, (including components of the study medication preparation), anesthetics or antibiotics or any other products associated with the treatment and general study procedures.
11. 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.
12. 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.
13. 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.
14. Patient is currently participating in, or has previously participated in another therapeutic or device study since exiting study 191622-515 or 191622-516.
15. Any study drug related or study treatment related serious adverse event (SAE) 191622-515 or 191622-516 in the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2009
Enrollment:	9
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:	28-04-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2010

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-08-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2012
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	EUCTR2009-009216-53-NL
CCMO	NL27110.029.09