A randomized, double-blind, placebo-controlled, parallel-group, multi-centre, Phase IIb, study to determine the effect of BXL628 in women with detrusor overactivity

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

Summary

ID

NL-OMON31547

Source
ToetsingOnline

Brief title
BXL628

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
overactive bladder

Research involving
Human

Sponsors and support

Primary sponsor: BioXell S.p.A.
Source(s) of monetary or material Support: Farmaceutisch bedrijf

Intervention

Keyword: BXL628, detrusor overactivity, overactive bladder

Outcome measures

Primary outcome

: Change from baseline in the bladder volume at the first involuntary

contraction following 4 weeks of treatment.

Secondary outcome

symptom severity measured by the number of micturitions, urgency (number of

episodes and severity according to the Urgency Perception Scale), nocturia and

incontinence episodes measured by the three-day diary, micturition frequency

per liter voided, largest single void, volume voided per micturition (collected

two days out of the three-day diary), urodynamic and uroflowmetry parameters,

patient*s perception of bladder condition

Study description

Background summary

In several *in vitro* and *in vivo* experiments, BXL628, a vitamin D3 analogue, has been shown to be able to maintain bladder function, and in particular to significantly decrease frequency and amplitude of spontaneous non voiding contractions without affecting the residual volume. Given that overactive bladder is characterized by the presence of unstable bladder contractions leading to the lower urinary tract symptoms, the drug should be effective in restoring a normal micturition pattern. Urodynamic tests are in this respect the most appropriate and objective examination to prove these hypotheses .

Study objective

the primary objective is to evaluate the effect of BXL628 on the bladder volume at the first involuntary contraction following 4 weeks of treatment; the secondary objectives are to determine the effect of BXL628 on symptom severity measured by a three-day micturition diary, uroflowmetry and cystometric parameters, patient*s perception of bladder condition, safety and tolerability

Study design

multi-centre, multi-national, double-blind, randomized, placebo-controlled, parallel-group study

Intervention

The study will be divided into three phases:
pre-screening/washout for patients on OAB treatment
medication free run-in (one week)
double-blind therapy (4 weeks)
Patients will be treated with: placebo or 75 mcg or 150 mcg of BXL628 (78 patients per group)

Study burden and risks

the assumption of a Vitamin D3 analogue (as BXL628), may cause an increase in calcium levels in blood and urine; anyway previous studies have shown that the higher dose of 150 mcg of BXL628 administered for 12 weeks, was safe and well tolerated without causing clinically relevant increase in serum calcium levels. In this study the levels of calcium in blood and urine will be carefully monitored. The risks of urinary tract infections associated to urodynamic tests are estimated to be not higher than 10%.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Women aged 18-75 years
- Patients must have had symptoms of overactive bladder (OAB) for at least 6 months
- Patients must exhibit all of the following symptoms during the three-day diary collecting period prior to start of treatment: frequency at least 8 times per 24 h, urgency at least once per 24 h with or without one episode of urge incontinence in 24h.
- Urodynamically confirmed detrusor overactivity. A urodynamic evaluation dated within 6 months before the enrolment can be considered valid
- Patients on anticholinergic /antispasmodic drugs for the treatment of OAB must discontinue this treatment at visit 1 (at least 14 days prior to visit 2).
- Women of childbearing potential should use two well established contraceptive methods (e.g. contraceptive pill and condom, IUD and condom) or abstain from sexual intercourse
- Patients must be capable of independent toileting
- Ability to fully understand all study procedures and to provide written informed consent to study participation
- Ability to comply with dosing and study visits scheduled for the duration of 1 month

Exclusion criteria

- Patients with predominant stress incontinence
- Patients with well established neurological disorder (e.g. Multiple Sclerosis, Parkinson*s disease, Alzheimer disease)
- Patients with pelvic organ prolapse staged III or IV (ICS classification)
- Patients who have undergone urogenital surgery such as hysterectomy less than 6 months prior to visit 1

- Painful bladder syndrome
- Patients with clinically significant bladder outlet obstruction and/or patients with a post void residual volume (PVR) ultrasound result, greater than 100 ml
- Patients with total daily volume greater than 2.8 l of voided urine
- History of acute urinary retention or history of repeated catheterizations due to acute urinary retention within the 3 months prior to visit 1
- Patients who intend to start a bladder training programme while in the study
- Patients with an indwelling catheter and patients practising intermittent self-catheterisation
- Patients who have undergone bladder biopsy or any other minor pelvic surgical intervention less than 30 days prior to visit 1
- Bladder cancer
- Patients with acute or recurrent urinary tract infection (UTI) and/or unexplained haematuria
- Stone in the bladder or urethra and upper tract stone disease causing symptoms
- Evidence of renal insufficiency (creatinine > 1.5 x upper limit of normal)
- Evidence of hepatic disease (total bilirubin > 1.5 x upper limit of normal, or AST or ALT or alkaline phosphatase > 2 x upper limit of normal)
- Patients with other clinically significant systemic diseases that may interfere with participation in this study
- Patients who are abusers of alcohol and/or other drugs
- History of disturbed calcium, phosphorus or magnesium metabolism
- Patients with allergy, hypersensitivity or other medical contraindications to Vitamin D
- Patients taking any of the following at any time during the study: Anticholinergic /antispasmodic drugs for the treatment of OAB; Calcitriol and other vitamin D analogs; Cholestiramine and other bile acid-binding resins; Cardiac glycosides; Drugs containing magnesium; Anticonvulsants; Estrogen treatment (unless started more than 2 months before randomization; estrogen containing oral contraceptives are allowed)
- Patients who have received any investigational drug during the preceding 90 days or 5 times the plasma half-life (if known), whichever is longer, or who have previously participated in this trial
- Patients unable and/or unlikely to comprehend and follow the study procedures and instructions
- Patients who intend to donate blood or blood products during the study or within one month following the completion of the study
- Patients who are pregnant or lactating

Study design

Design

Study phase:	2
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):	05-08-2008
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine

Ethics review

Approved WMO Date:	06-09-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-04-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-07-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-07-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-07-2008

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2007-001214-16-NL
CCMO	NL17609.041.07