A RANDOMISED, MULTI-CENTRE, DOUBLE-BLIND, PLACEBO- AND ACTIVE-CONTROLLED, 5-WAY, PARALLEL GROUP STUDY TO INVESTIGATE THE EFFICACY, SAFETY AND TOLERABILITY OF ONO-8539 IN PATIENTS WITH OVERACTIVE BLADDER

Published: 24-12-2008
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The primary objective of this trial is to compare the effect of three different doses of ONO-8539 with placebo in the mean change of the number of micturitions per 24 hrs from baseline to 12 weeks.The secondary objectives of this trial will be:*To...

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

Summary

ID

NL-OMON33831

Source
ToetsingOnline

Brief title
Emerald

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
overactive bladder/ urine incontinence

Research involving

Human

Sponsors and support

Primary sponsor: ONO Pharma
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Overactive bladder, Prostaglandin E2, Urge incontinence

Outcome measures

Primary outcome

The primary efficacy endpoint is the mean change from baseline in the number of micturitions per 24 hrs at 12 weeks.

Secondary outcome

The secondary efficacy endpoints are:

* % change from baseline in the number of micturitions per 24 hrs at 2, 4, 8 and 12 weeks.
* Mean change from baseline in the number of micturitions per 24 hrs at 2, 4 and 8 weeks (and at 12 weeks for Tolterodine (Detrusitol® XL) versus placebo) .
* Mean and % change from baseline in the number of urinary urgency incontinence (UUI) episodes per 24 hrs at 2, 4, 8 and 12 weeks.
* Mean and % change from baseline in the number of urgency episodes per 24 hrs at 2, 4, 8 and 12 weeks.
* Mean and % change from baseline in most frequent severity of urinary urgency at 2, 4, 8 and 12 weeks.
* Mean and % change from baseline in the number of continent days per week

(among incontinent patients) at 2, 4, 8 and 12 weeks.

* Mean and % change from baseline in the volume voided per micturition at 2, 4,

8 and 12 weeks

* Mean and % change from baseline in the number of micturitions during daytime

at 2, 4, 8 and 12 weeks.

* Mean and % change from baseline in the number of micturitions during sleeping

time (nocturia) at 2, 4, 8 and 12 weeks.

* Responder analysis

* Treatment response

* Patient perception of bladder condition (PPBC) and bother scale (ICIQ-OAB).

* Quality of life using the King*s Health Questionnaire.

Study description

Background summary

Overactive bladder (OAB) is defined as urgency, with or without urgency incontinence, usually with frequency and nocturia if there is no proven infection or other obvious pathology. It is a commonly occurring complex of symptoms that affects about 16% of the adult population in Europe and the US. The prevalence of OAB increases with age and is similar in men and women. It is estimated that there are approximately 22 million adults (> 40 years old) affected by OAB in Europe.
The current treatment for OAB focuses on the use of anticholinergic drugs which are contraindicated in patients with bladder outlet obstruction and glaucoma. Dry mouth also seems to be a cause of patient non-compliance to chronic anticholinergic treatment. Thus EP1 receptor antagonists, may offer efficacious treatment for OAB, without the adverse effects or contraindications seen with anticholinergic drugs.

The hypothesis for this study is that one or more of the investigative doses of ONO-8539 will lead to a mean relative decrease in the number of micturitions per 24 hrs of at least 1.5 compared to placebo at 12 weeks and controlling for

baseline.

Study objective

The primary objective of this trial is to compare the effect of three different doses of ONO-8539 with placebo in the mean change of the number of micturitions per 24 hrs from baseline to 12 weeks.

The secondary objectives of this trial will be:
*To compare the effect of three different doses of ONO-8539 and Tolterodine (Detrusitol XL) versus placebo on the number of micturitions per 24 hrs, frequency of urinary urgency incontinence episodes per 24 hrs, number of urgency episodes per 24 hrs, severity of urgency, mean volume voided per micturition, number of micturitions during daytime, number of micturitions during sleeping time, and number of continent days (among incontinent patients) during the course of treatment.
*To compare the effect of three different doses of ONO-8539 and Tolterodine (Detrusitol XL) versus placebo on subjective scales of treatment effect and Quality of Life during the course of treatment.
*To compare the safety and tolerability of three different doses of ONO-8539 and Tolterodine (Detrusitol XL) versus placebo.

In addition, the exploratory objectives of this trial will be:
*To investigate the dose response of ONO-8539.
*To investigate the plasma concentration of ONO-8539 and its glucuronide.
*To investigate the association between the changes in efficacy parameters of ONO-8539 and the plasma concentrations of ONO-8539.
*To investigate the association between the changes in efficacy parameters of ONO-8539 and baseline level/post-treatment level of PGE2 in urine.
*To compare the efficacy and safety between the three different doses of ONO-8539 versus Tolterodine (Detrusitol XL).
*To undertake subgroup analyses using appropriate clinical and biological factors.

Study design

Randomised, double-bllind, placebo- and active-controlled, 5-way parallel group.

Intervention

Patients will take their morning dose (six tablets of ONO-8539 and/or matching placebo, and one capsule of Tolterodine or matching placebo) after breakfast and take their evening dose (six tablets of ONO-8539 and/or matching placebo) after dinner.

Patients will receive the following:
One of three possible treatment doses of ONO-8539 - either 30mg twice a day, 100 mg twice a day or 300mg twice a day- or Tolterodine 4mg once daily or Placebo. ONO-8539 is available in tablets of 10 mg and 50 mg. This results in the following:

- Placebo group: Twice a day 6 placebo tablets of ONO and once a day Tolterodine placebo capsule.
- Ono 30 mg group: Twice a day 3 tablets of 10 mg and 3 placebo tablets and once a day Tolterodine placebo capsule.
- Ono 100 mg group: Twice a day 2 tablets of 50 mg and 4 placebo tablets and once a day Tolterodine placebo capsule.
- Ono 300 mg group: Twice a day 6 tablets of 50 mg and once a day Tolterodine placebo capsule.
- Tolterodine 4 mg group: Twice a day 6 placebo tablets of ONO and once a day Tolterodine capsule.

Study burden and risks

Burden for the patient:
- Patients have to come in 7 times.
- Patients have to complete a bladder diary 3 days before every visit.
- Every day a compliance diary must be completed
- 3 times a physical examination
- 2 times completion of questionnaire
- 3 times uro-flow (Qmax) for all man and for women only if there is a clinical relevance.
- 4 times ECG
- Blood will be drawn 7 times 20 ml.

Gastrointestinal side effects such as nausea, diarrhoea, heartburn and abdominal pain were reported occasionally. Other side effects are headache, decreased appetite, urinary frequency, sweating, rash and sleepiness.

Contacts

Public
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Scientific
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JAPAN

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) medical history of OAB symptoms with urinary urgency for >6 months prior to screening
2) during the placebo run-in phase a) >8 micturitions per 24 hrs, and either b) >1 urgency episode per 24 hrs and >6 urgency episode per 72 hrs or c) >1 urinary urgency incontinence episode per 24 hrs (on each day recorded in the 3-day diary period).

Exclusion criteria

History of lower urinary tract pathology that could be responsible for urgency or incontinence (e.g. genuine stress incontinence, bladder stones, interstitial cystitis, urothelial tumours), neurogenic detrusor overactivity and urinary tract infections.

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):	15-07-2009
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	-
Product type:	Medicine
Brand name:	Detrusitol XL
Generic name:	Tolterodine tartrate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	24-12-2008
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	23-03-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-04-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	10-09-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	15-09-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	30-11-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	02-12-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	30-12-2009
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	12-01-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2007-006538-33-NL
CCMO	NL25989.098.08