A phase II, randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of Org 3236 tablets in men with Lower Urinary Tract Symptoms (LUTS) suggestive of Benign Prostatic Hyperplasia (BPH)

Published: 25-01-2008
Last updated: 07-05-2024

The objectives are to evaluate:- The effect of Org 3236 on prostate volume compared to placebo;- The effect of Org 3236 on LUTS compared to placebo;- The effect of Org 3236 on urinary flow and postvoid residual volume compared toplacebo;- The effect...

Ethical review	Approved WMO
Status	Pending
Health condition type	Urinary tract signs and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON31439

Source
ToetsingOnline

Brief title
Efficacy- and safety trial in men with LUTS/BPH

Condition

- Urinary tract signs and symptoms

Synonym
prostate hyperplasia

Research involving

Human

Sponsors and support

Primary sponsor: Organon Nederland BV
Source(s) of monetary or material Support: door de opdrachtgever

Intervention

Keyword: BPH, Efficacy, LUTS, Safety

Outcome measures

Primary outcome

Prostate volume (total and transition zone) will be measured using transrectal ultrasound (TRUS). In addition, as a biomarker for prostate volume PSA will be measured.

The effect on LUTS will be evaluated by using the seven questions of the International Prostate Symptom Score (IPSS).

Urinary flow (Qmax and Qav) will be measured using an automatic uroflow meter.

Postvoid residual volume will be measured using transabdominal ultrasound.

Progression of LUTS is defined as occurrence of either 1) Acute Urinary Retention (AUR), 2) need for Transurethral Resection of Prostate (TURP) or other minimal invasive therapy or 3) worsening of symptoms defined as IPSS increase of >= 4 points

compared to baseline. The first two will be assessed by means of (serious)

adverse

event reporting.

Sexual function, well-being and LUTS-related QoL will be assessed by the Benign Prostatic Hypertrophy-Related Quality of Life Questionnaire (BPH-QoL9), the Male Sexual Health Questionnaire to assess Ejaculatory Dysfunction (MSHQ-EjD Short Form), and the IPSS-Quality of Life question.

Safety will be evaluated by monitoring (serious) adverse events, vital signs,

and by

determination of (routine) laboratory parameters.

A population PK-PD analysis will be performed using the non-linear mixed effects modeling approach to characterize a.o. the relationship between Org 3236 serum concentrations, testosterone serum concentrations and total prostate volume.

Secondary outcome

Niet van toepassing

Study description

Background summary

Benign prostatic hyperplasia (BPH) is a common disorder in the elderly male population that is characterized by a progressive enlargement of prostatic tissue,
resulting in obstruction of the proximal urethra and causing urinary flow

disturbances.
Currently, pharmacological treatment of Lower Urinary Tract Symptoms suggestive of
Benign Prostatic Hyperplasia (LUTS/BPH) mainly consists of α-adrenergic inhibitors
or 5α-reductase inhibitors, but also the combination of these inhibitors has been
investigated.
The α-adrenergic inhibitors relieve the obstructed urinary flow and consequently symptoms by relaxing the smooth muscle in the prostate (act on the dynamic component). Because α-blockers have a good symptom relief with a fast time to onset (within days), these are often the first choice of treatment, particularly in men
with smaller prostates. However, these blockers delay but do not reduce the longterm
risk of acute urinary retention (AUR) and the need for invasive surgery.
5α-Reductase inhibitors block the 5α-reduction of testosterone to the more potent
dihydrotestosterone (DHT), and by this pathway prostate volume is reduced and symptoms relieved. 5α-Reductase inhibitors are mainly prescribed in patients with
larger prostates (>40 mL). Compared to α-blockers, time to onset of action is longer and symptom relieve is less, however, long term risk of acute urinary retention and need for invasive surgery are smaller.
Combination therapy of α-blockers and 5α-reductase inhibitors has been shown to be
effective in improving symptom scores and preventing clinical progression of BPH. One single compound with fast onset of action (faster than 5α-reductase inhibitors)
and prevention of clinical progression would be an improvement to currently available BPH therapies. Intermittent therapy with Gonadotropin Releasing Hormone (GnRH) antagonists might provide such improvement.

Suppression of testosterone to the low normal range can also be achieved by progestins as has been shown in the broad male contraception experience. In addition, progestins are well tolerated in men.

Allylestrenol is a progestin that has been approved for the indication BPH in Japan.
Etonogestrel (ENG, Org 3236) is the active metabolite of desogestrel (DSG), and has
been used in female contraceptives since 1981. Both ENG and DSG in combination with testosterone pellets or injections have been studied in males as a potential male
hormonal contraceptive. Also some data are available on DSG and Org 3236 alone in males
In conclusion, both 150 and 300 µg DSG or Org 3236 provide testosterone

suppression to a level that has been proven to be effective and safe for intermittent
treatment of LUTS/BPH, as shown by the two GnRH antagonists and allylestrenol. In the current protocol an explorative clinical trial is described to test this concept of
Org 3236 (ENG) for LUTS/BPH.

Study objective

The objectives are to evaluate:
- The effect of Org 3236 on prostate volume compared to placebo;
- The effect of Org 3236 on LUTS compared to placebo;
- The effect of Org 3236 on urinary flow and postvoid residual volume compared to
placebo;
- The effect on progression of LUTS;
- The effect of Org 3236 on sexual function, well-being and LUTS-Life compared to placebo;
- The safety of Org 3236;
- The pharmacokinetic (Org 3236) and pharmacodynamic (T, DHT, SHBG) properties.

The effects will be evaluated during treatment and post-treatment.

Study design

This is a randomized, double-blind, placebo-controlled, comparative, multiple dose trial in 240 subjects with LUTS/BPH. Subjects will be randomly to one of the following regimens (60 subjects per treatment group):
Group 1: 150 µg Org 3236 per two days
Group 2: 150 µg Org 3236 per day
Group 3: 300 µg Org 3236 per day
Group 4: placebo

Treatment duration is eight weeks with a follow up period of 16 weeks.

Study burden and risks

RISKS AND DISCOMFORTS
Because of the anticipated reduction of testosterone concentration in the blood, effects related to too low testosterone concentrations may occur during the treatment
period. These include libido decrease, reduced production of sperm, mood effects (like short temper, emotional lability, depression, and tiredness), increased sweating,
hot flushes, slight breast enlargement, and mild anemia. These effects are

expected
to recover soon after treatment cessation. Moreover, possible effects related to Etonogestrel may occur, like weight gain and a transient decrease of a subtype of
cholesterol, i.e. High Density Lipoprotein (HDL) Cholesterol which is also called the
good cholesterol.
Possible side effects from blood drawing include faintness, swelling of the vein, pain,
bruising or bleeding at the site of puncture. There is also a slight possibility of
infection at the site where blood was drawn.
The assessment of the prostate volume for which a small probe is placed into the rectum (transrectal ultrasound) may be experienced as unpleasant. In addition, if a
prostate biopsy is needed to exclude prostate cancer, this may also cause discomfort.

POTENTIAL BENEFITS
The urinary complaints may improve and the prostate volume may reduce as a result of
the treatment. Participation in the trial may provide useful information that will help
individuals having a similar medical condition.

Contacts

Public
Organon Nederland BV

Griekenweg 25
5342 PX Oss
Nederland
Scientific
Organon Nederland BV

Griekenweg 25
5342 PX Oss
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Men diagnosed with LUTS suggestive of BPH
- Age at least 50 but not older than 80 years at screening
- PSA < 10 ng/mL and exclusion of prostate cancer to the satisfaction of the investigator

Exclusion criteria

- A postvoid residual volume >250 mL
- Use of anti-androgens, androgens, Gonadotropin Releasing Hormone (GnRH) antagonists, or 5alfa-reducatase inhibitors within six months prior to start trial medication
- Presence of hypogonadism as judged by the investigator
- Acute urinary retention within the past 12 months
- History of surgery for BPH, including other minimally invasive procedures
- Presence of urinary tract infection
- Presence or history of (subclinical) prostate cancer, bladder cancer, urethral stricture, or pelvic irradiation
- Presence or history of any neurological disease associated with primary bladder dysfunction.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2008
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	etonogestrel
Generic name:	etonogestrel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	25-01-2008
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2007-005793-31-NL
CCMO	NL21014.091.08
Other	zie www.organontrials.com