A MULTI-CENTER, RANDOMIZED, CROSS-OVER, DOUBLE-BLIND, THIRD PARTY OPEN, PLACEBO CONTROLLED, PILOT STUDY TO ASSESS THE URODYNAMIC EFFECTS OF MODIFIED RELEASE UK-369,003 IN MEN WITH LOWER URINARY TRACT SYMPTOMS (LUTS)

Published: 29-12-2006
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A pilot study to:1. assess the urodynamic changes induced by 100mg MR formulationof UK-369,003 vs. placebo in men with LUTS;2. Assess the safety and tolerability of UK-369,003 in men with LUTS

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Urinary tract signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON30658

Source
ToetsingOnline

Brief title
The effects of UK-369,003 MR on urodynamics in patients with LUTS

Condition

- Urinary tract signs and symptoms

Synonym
miction problems

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer

Intervention

Keyword: 003, Lower urinary tract symptoms, LUTS, UK-369

Outcome measures

Primary outcome

* PdetQmax (detrusor pressure at maximum flow rate)

* Qmax

* Cystometric capacity

* Post-void residual urine volume (PVR)

* Qave (average flow rate)

This is calculated as follows: Average flow rate = volume voided/flow time

* Volume at first unstable contraction. This may not occur in all patients

* Average detrusor pressure during micturition

* BOOI (bladder outlet obstruction index; formerly the Abrams-Griffiths number)

This is calculated as follows: PdetQmax *2Qmax

* BCI (bladder contractility index)

This is calculated as follows: PdetQmax +5Qmax

* BE (Bladder voiding efficiency)

This is calculated as follows: (Voided volume/cystometric capacity) X 100

* Frequency of unstable contractions

(An unstable contraction is defined as: an involuntary increase in detrusor

pressure

during bladder filling of * 5cmH20)

* Mean amplitude of unstable contractions

(An unstable contraction is defined as: an involuntary increase in detrusor

pressure

during bladder filling of * 5cmH20)

Secondary outcome

* Patient Reported Treatment Impact (PRTI)

* International Prostate Symptom Score (IPSS)

Study description

Background summary

UK-369,003 is a highly selective and potent inhibitor of Phosphodiesterase (PDE) 5.
UK-369,003 has negligible activity against PDEs 1-4 and 7-11 (IC50*s >2000 nM cf.
IC50 of 1.4 nM against human corpus cavernosum derived PDE5). It has increased selectivity for PDE5 over PDE6 (>80 fold) compared to sildenafil (~10 fold). Two recently completed studies (A3711029 and A3711030) have demonstrated efficacy in treating ED. UK-369,003 improves ED by reducing the catabolism of cGMP by PDE5, enhancing smooth muscle relaxation of the corpus cavernosum. UK-369,003 was well tolerated in both studies.
(Further information is available in the UK-369,003 investigator*s brochure.)

Study objective

A pilot study to:
1. assess the urodynamic changes induced by 100mg MR formulation of UK-369,003 vs. placebo in men with LUTS;
2. Assess the safety and tolerability of UK-369,003 in men with LUTS

Study design

A multi-center double blind, randomized, placebo-controlled, third party open,

crossover phase II pilot study with two treatment arms. Following a washout period of up to 4-weeks subjects will undergo a baseline assessment (BL) of their bladder storage and voiding function. They will then be randomized (1:1 ratio) to either once daily 100mg MR UK-369,003 or placebo for a minimum of 2 weeks. The subjects will then have an end of first treatment period (EOT1) pressure flow study assessment. This will be followed by a 2-4 week washout period. The subjects will then attend for period 2. At the beginning of treatment period (BOT2) subjects will attend the clinic to receive medication and complete patient outcome measures but will not undergo any urodynamics. After receiving study treatment for a minimum of 2 weeks an end of second treatment period (EOT2) pressure flow study assessments will be conducted. This will be followed by a follow-up visit 1 week after the EOT2 which in the absence of adverse events, may be conducted by phone.
Interim analyses may be conducted as the study is ongoing. These will be performed by a third party at Pfizer. The results of these analyses will not enable individuals directly involved in the execution of the study (such as the investigators, sponsor*s operational team and central urodynamics reader) to identify treatment assignments for subjects until after the study is completed.

Intervention

Formulation and Packaging
UK-369,003 will be supplied as 50mg Modified Release tablets presented as blue and white, round bilayer tablets. Matching placebo will be provided.
Each dose will consist of 2 tablets of either 50mg Modified Release or placebo to
match. Sufficient supplies for 2 weeks with up to 7 days overage will be provided so that if it is necessary for subjects to re-arrange a planned clinic visit they may do so and still continue receiving medication.

Administration
Subjects will take two tablets orally with a glass of water every morning. These must be swallowed whole, one after the other, and without chewing.

Study burden and risks

UK-369,003 is similar to a drug known as sildenafil (Viagra®). These drugs work by inhibiting an enzyme (a chemical substance found in the body) present in the penis (known as PDE5). Results from tests, some of which used animals, show that the same chemical pathway that the body uses for relaxing muscles around the penis that enables an erection to take place may also affect tissues in the body used to control urination. Therefore some of the side effects of UK-369,003 may be similar to those seen with Viagra®.

SIDE EFFECTS
Thus far, UK-369,003 has been administered to over 1200 patients and healthy

volunteers at different dosages. Based on research studies and the experience of other people who have received UK-369,003 some side effects may occur. UK369,003 has been well tolerated with the most common side effects being headache, vasodilatation (flushes), rhinitis (nasal congestion), dyspepsia, erections, dizziness, muscular pain and back pain.
All these effects were generally short term and weak to moderate in intensity. Additional side effects include: changes in colour vision, conjunctivitis and diarrhea. Although these events were reported during treatment with UK369,003, they were not necessarily caused by it.
As with all new drugs there may be unforeseen side effects but we do not expect you to suffer any health problems by taking part in this study. If any significant facts or side effects appear during this study, you will be notified.
Some new problems or side effects could happen; if this should occur, you will be told of any changes in the way the study is done. You will also be told of any new risks or side effects. This information may affect your decision about continuing in the study.
You will be informed as soon as possible of any new findings relevant to this study.

DISCOMFORTS
Some men may find bladder filling and catheterization uncomfortable although they should not be painful. You may have some discomfort passing urine for 1 or 2 days after the procedure and may also notice some blood in your urine; this is normal. If the discomfort is considerable or lasts longer than 2 days, then please speak with the study doctor. There is small risk of urinary tract infection after bladder filling which can be treated with antibiotics.

POSSIBLE BENEFITS OF THE STUDY
You will get study drug and all medical treatment in this study at no cost to you. You may have a good response to the treatment. Others may benefit from the information learned from the study. It is also possible that you will receive no direct health benefit from being in this study.

Contacts

Public
Pfizer

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Nederland
Scientific
Pfizer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

age <=> 40 years
LUTS with definition IPSS <=> 13 score
with clinical diagnosis of BPH
(see protocol page 13)

Exclusion criteria

prostate cancer
documentation of urine infection
use of certain medication(s) and/or operation(s)
(see protocol 13-16)

Study design

Design

Study phase:	2
Study type:	Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2007
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	niet van toepassing

Ethics review

Approved WMO Date:	29-12-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-03-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2007
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2008
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	EUCTR2006-004380-58-NL
CCMO	NL15243.029.06