A Phase 2, Randomised, Double-Blind, Placebo-Controlled Trial to Investigate the Safety and Efficacy of AV608 in Subjects with Idiopathic Detrusor Overactivity

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To evaluate the urodynamic effects, the safety and tolerability and the clinical efficacy of AV608 compared with placebo in subjects with idiopathic detrusor overactivity

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

Summary

ID

NL-OMON29909

Source
ToetsingOnline

Brief title
AV608-106 Idiopathic Detrusor Overactivity, 7 February 2006

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
Idiopathic Detrusor Overactivity, Overactive bladder

Research involving
Human

Sponsors and support

Primary sponsor: Avera Pharmaceuticals
Source(s) of monetary or material Support: Avera Pharmaceuticals Inc.

Intervention

Keyword: AV608, cystometric bladder measurements, Neurokinin antagonist, Overactive bladder syndrome

Outcome measures

Primary outcome

The primary efficacy outcome is a comparison between treatment groups of the

change from baseline in maximum cystometric bladder capacity (mL).

Secondary outcome

Four contraction variables measured during cystometry.

Bladder sensation, including the volume at first sensation, the volume at

normal desire and the volume at strong desire to void.

Urgency, frequency and urge incontinence events as recorded in the Subject

Micturition Diary.

Urgency Perception Scale and Patient Global Impression of Change.

Study description

Background summary

Presently, medications available for OAB have tolerability limitations which cause unpleasant side effects. There are currently very few alternatives for those patients who either do not respond to or cannot tolerate these medications.
Based on the earlier studies, it is believed that AV608 will reduce or even fully suppress the symptoms of an overactive bladder by blocking the receipt of the improper messages from the bladder to the brain. In these earlier studies, AV608 has been well tolerated and demonstrated a favorable safety profile with

the majority of adverse events being mild and transient.

Study objective

To evaluate the urodynamic effects, the safety and tolerability and the clinical efficacy of AV608 compared with placebo in subjects with idiopathic detrusor overactivity

Study design

This is a randomized, double-blind, placebo-controlled trial. The trial will be conducted at approximately 12 sites in the European Union (EU).
Subjects who provide written informed consent will be screened to ensure they satisfy all inclusion and exclusion criteria. The screening period may last from 4 to 28 days, depending on the need to wash out prohibited medications prior to randomization. Subjects will return to the study site at the end of the screening period (Visit 2) for the qualifying urodynamic assessment followed by randomization, if appropriate.
Approximately 62 subjects will be randomized to receive either AV608 or placebo in a 1:1 ratio. The double-blind treatment period for each subject will last for 3 weeks. All subjects will take 80 mg/day of AV608 or placebo for 3 days and then take 160 mg/day of AV608 or placebo thereafter. At the end of the treatment period (Visit 3), subjects will return to the study site and complete a second urodynamic assessment.
All subjects will return to the study site approximately 1 week after the last dose of trial medication for a final Follow Up Visit (Visit 4).

Study burden and risks

The maximum duration of the study for each subject is 56 days. The 4 clinic visits will involve about 11 hours attendance in total. Two blood samples will be taken and 2 urodynamic assessments performed.
Repeated catheterisation, as is needed for cystometry, does carry a risk of bladder infection. To reduce this risk after the cystometry a single oral dose of a common antibiotic is given as a preventative measure.
The treatment used in this study may cause some or no side effects which include tiredness, headache, blocked nose and sore throat, nausea, feeling dizzy when standing up, and sleepiness. In previous studies, the majority of side effects were mild and did not last long. In addition, there is always a risk that some very uncommon or unknown side effects may occur.
This is a proof of concept study and if successful would provide a strong rationale to study this treatment further in the clinical management of OAB.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Female, 18 to 65 years of age, inclusive. Individuals outside this age range will not be included in line with standard clinical trial practice.
2)A current primary diagnosis of OAB consistent with idiopathic detrusor overactivity with symptoms present for at least 6 months prior to Screening.
3)Idiopathic detrusor overactivity, demonstrated by a urodynamic observation, which is characterized by involuntary detrusor contraction during the filling phase and is associated with a sensation of urgency.
4)Evidence of frequency (greater than 8 micturitions/24 hours) in combination with urinary urgency during the 7 days prior to baseline (Visit 2) based on the micturition diary.
5)Willingness to participate in this study as evidenced by a signed, written informed consent form (ICF).
6)If of child*bearing potential (i.e., not post*menopausal or documented to be surgically

sterile) willingness to avoid pregnancy and practice adequate birth control (e.g., oral contraception, intrauterine devices, implantable devices, depot contraceptives, double barrier method) from the time of study enrollment through at least 30 days after the final dose of study medication.
7)Negative serum pregnancy test at Visit 1 (Screening) and negative urine pregnancy test at Visit 2 (Randomisation).
8)Agrees to refrain from blood donation during the course of the study.

Exclusion criteria

1) Subjects who are pregnant or lactating.
2) Clinically significant abnormality or clinically significant unstable medical condition as indicated by medical history, physical examination, ECG results, clinical laboratory testing, or the investigator's judgment at Screening (Visit 1) or Baseline (Visit 2).
3) QTc interval of 470 msec or greater at Screening (Visit 1).
4) Predominant stress urinary incontinence versus urge urinary incontinence based on subject history.
5) Neurogenic bladder (e.g. associated with spinal cord injury, multiple sclerosis, etc.).
6) Post micturition volume of >100 mL at baseline assessment.
7) Maximum bladder capacity > 400 mL at baseline assessment.
8) Anatomic or structural abnormalities possibly causing urinary incontinence or urgency,including but not limited to urogenital prolapse stage 2 or more according to the Pelvic Organ Prolapse Quantification (POP*Q) system.
9) Current UTI or frequent UTIs (i.e., greater than 4 UTIs per year), interstitial cystitis, hematuria of unknown cause, or use of indwelling catheter.
10) Urological or gynecological surgery within 3 months of the baseline urodynamic assessment; cystoscopy within 30 days of the baseline urodynamic assessment.
11) Electro*stimulation therapy, bladder training, or physiotherapy for bladder control within 2 weeks of Screening (Visit 1).
12) History (within 1 year of Screening) of alcohol or substance dependence (except nicotine dependence) according to DSM*IV*TR criteria.
13) History of any kind of cancer within the last 2 years.
14) Existing non*malignant tumors that could compromise the function and/or anatomy of the lower urinary tract.
15) Subjects who have taken any prohibited medications within two weeks of baseline (Visit 2) or have any anticipated need or intended use of these medications during the study. Prohibited medications include, but are not limited to, oxybutynin, tolterodine, duloxetine, trospium chloride, darifenacin, solfenacin, and herbal preparations.
16) Participation in any clinical trial within the past 3 months (for investigational drugs, products, or devices).
17) Subjects who have previously received AV608 (previously known as NKP*608).
18) Positive result on urine testing for drugs of abuse (cannabis, amphetamines, cocaine, and phenycylidine) at Screening (Visit 1).
19) Any past or present history of liver disease (with the exception of history of hepatitis A) or renal failure (creatinine clearance < 60 cc/minute).

20) Current hypothyroidism or hyperthyroidism or laboratory findings consistent with thyroid dysfunction. Subjects who are being treated for thyroid disorder are eligible if they have been on stable doses of thyroid hormone for at least 6 months prior to Screening (Visit 1) and are currently euthyroid.
21) Any other condition that, in the opinion of the investigator, would jeopardise the safety or rights of a subject participating in the trial or would render the subject unable to comply with the protocol.
22) Members of the investigative staff or their families.

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:	Recruitment stopped
Start date (anticipated):	21-11-2006
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	none
Generic name:	none

Ethics review

Approved WMO Date:	21-04-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-06-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-08-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-08-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-09-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-11-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-12-2006
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-05-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-06-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	29-06-2007
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	EUCTR2005-005868-93-NL
CCMO	NL11405.041.06