A Randomized, Double-Blind, Parallel-Group, Active-Controlled, Multi-center Study to Evaluate the Long-Term Safety and Efficacy of Combination of Solifenacin Succinate with Mirabegron Compared to Solifenacin Succinate and Mirabegron Monotherapy in Subjects with Overactive Bladder

Published: 25-11-2013
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Primary objective:* To evaluate the safety and tolerability of long-term combination treatment with solifenacin (5 mg)with mirabegron (50 mg) compared to solifenacin and mirabegron monotherapySecondary objectives:* To evaluate efficacy of long-term...

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

Summary

ID

NL-OMON41508

Source
ToetsingOnline

Brief title
SYNERGY II (178-CL-102)

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
overactive bladder

Research involving
Human

Sponsors and support

Primary sponsor: Astellas Pharma
Source(s) of monetary or material Support: Industry

Intervention

Keyword: mirabegron, Overactive bladder, Solifenacin succinate

Outcome measures

Primary outcome

Primary

Incidence and severity of treatment emergent adverse events (TEAEs)

Primary Efficacy Variables

* Change from baseline in mean number of incontinence episodes per 24 hours at

EoT

* Change from baseline in mean number of micturitions per 24 hours at EoT

Key Responder Variables

* Zero Incontinence Episodes: a responder is defined as a subject with 0

incontinence episodes

post-baseline in the last 3 days prior to Month 1, 3, 6, 9, 12, and EoT

* Responders for changes from baseline in Symptom Bother and health related QoL

scores as

assessed by OAB-q: a responder is defined as a subject with at least 10 points improvement from baseline to each visit (Month 1, 3, 6, 9, 12, and EoT)

* 50% Reduction in Incontinence Episodes: a responder is defined as a subject with at least 50% decrease from baseline in mean number of incontinence episodes per 24 hours (Month 1, 3, 6, 9, 12, and EoT)

Secondary outcome

Secondary Safety Variables

* Vital signs: sitting systolic and diastolic blood pressure and pulse rate (home measurements and office measurements)
* Laboratory tests: hematology, biochemistry, and urinalysis
* ECG parameters
* PVR

Secondary Efficacy Variables

* Change from baseline in mean volume voided per micturition at EoT
* Change from baseline in Symptom Bother as assessed by Overactive Bladder Questionnaire (OAB-q) at EoT
* Change from baseline in subject assessment of Treatment Satisfaction * Visual Analogue Scale

(TS-VAS) at EoT

* Number of incontinence episodes at Month 1, 3, 6, 9 12, and EoT and changes from baseline

* Change from baseline in mean number of incontinence episodes at secondary time points (after 1, 3, 6, 9 and 12 months of treatment)

* Change from baseline in mean number of micturitions at secondary time points (after 1, 3, 6, 9 and 12 months of treatment)

* Change from baseline in mean volume voided at secondary time points (after 3, 6 and 12 months of treatment)

* Number of urgency incontinence episodes during the 7-day observation period prior to Month 1, 3, 6, 9, 12, and EoT and changes from baseline

* Change from baseline in mean number of urgency incontinence episodes per 24 hours (Month 1, 3, 6, 9, 12, and EoT)

* Change from baseline in mean number of urgency episodes (grade 3 and/or 4)/24 hours (PPIUS scale) (Month 1, 3, 6, 9, 12, and EoT)

* Number of nocturia episodes during the 7-day observation period prior to Month 1, 3, 6, 9, 12, and EoT and changes from baseline

* Change from baseline in mean number of nocturia episodes per 24 hours (Month

1, 3, 6, 9, 12,

and EoT)

* Number of pads used during the 7-day observation period prior to Month 1, 3,

6, 9, 12, and EoT

and changes from baseline

* Change from baseline in mean number of pads used per 24 hours (Month 1, 3, 6,

9, 12, and EoT)

* Number of incontinence-free days during the 7-day diary period (Month 1, 3,

6, 9, 12, and EoT)

* Number of days with less than 8 micturitions during the 7-day diary period

(Month 1, 3, 6, 9, 12,

and EoT)

* Number of incontinence-free days with less than 8 micturitions during the

7-day diary period

(Month 1, 3, 6, 9, 12, and EoT)

* Change from baseline in PPBC (Month 1, 3, 6, 9, 12, and EoT)

* Change from baseline in Symptom Bother as assessed by the OAB-q at secondary

time points

(Month 1, 3, 6, 9, and 12)

* Change from baseline in health related QoL scores as assessed by the OAB-q

(including

subscales) (Month 1, 3, 6, 9, 12, and EoT)

* Patient Global Impression of Change (PGIC) scale (Month 12 and EoT)

* Change from baseline in scores as assessed by the European Quality of Life in

5 Dimensions

(EQ-5D) questionnaire (including subscales) (Month 1, 3, 6, 9, 12, and EoT)

* Change from baseline in scores as assessed by the Work Productivity and

Activity Impairment:

Specific Health Problem (WPAI:SHP) questionnaire (Month 6, 12, and EoT)

* Change from baseline in the subject's assessment of TS-VAS at secondary time

points (Month 1,

3, 6, 9, and 12)

Other Responder Variables

* Micturition Frequency Normalization: a responder is defined as a subject who

had at least 8

micturitions per 24 hours at baseline and less than 8 micturitions per 24 hours

post-baseline

(Month 1, 3, 6, 9, 12, and EoT)

* Zero Incontinence Episodes: a responder is defined as a subject with 0

incontinence episodes

post-baseline in the last 7 days prior to Month 1, 3, 6, 9, 12, and EoT

* Subjects with at least 1 point improvement from baseline in PPBC (Month 1, 3,

6, 9, 12, and EoT)

* Subjects with major (at least 2 points) improvement from baseline in PPBC

(Month 1, 3, 6, 9, 12,

and EoT)

* Double responder: 50% reduction in mean number of incontinence episodes per

24 hours

compared to baseline and MID reached (improvement by at least 10 points) on the

Symptom

Bother scale of the OAB-q (Month 1, 3, 6, 9, 12, and EoT)

* Double responder: 50% reduction in mean number of incontinence episodes per

24 hours

compared to baseline and MID reached (improvement by at least 10 points) on the

HRQL Total

score of the OAB-q (Month 1, 3, 6, 9, 12, and EoT)

* Double responder: 50% reduction in mean number of incontinence episodes per

24 hours

compared to baseline and at least 1 point improvement from baseline in PPBC

(Month 1, 3, 6, 9,

12, and EoT)

* Triple responder: 50% reduction in mean number of incontinence episodes per

24 hours

compared to baseline, MID reached (improvement by at least 10 points) on the

Symptom Bother

scale of the OAB-q, and at least 1 point improvement from baseline in PPBC

(Month 1, 3, 6, 9,

12, and EoT)

* Triple responder: 50% reduction in mean number of incontinence episodes per

24 hours

compared to baseline, MID reached (improvement by at least 10 points) on the

HRQL Total score

of the OAB-q, and at least 1 point improvement from baseline in PPBC (Month 1,

3, 6, 9, 12, and

EoT)

Study description

Background summary

To evaluate the safety and tolerability of long-term combination treatment with solifenacin (5 mg)
with mirabegron (50 mg) compared to solifenacin and mirabegron monotherapy

Study objective

Primary objective:
* To evaluate the safety and tolerability of long-term combination treatment with solifenacin (5 mg)
with mirabegron (50 mg) compared to solifenacin and mirabegron monotherapy
Secondary objectives:
* To evaluate efficacy of long-term combination treatment with solifenacin and mirabegron
* To evaluate Patient Reported Outcomes (PRO) during long-term combination treatment with
solifenacin and mirabegron

Study design

This is a multinational, multi-center, randomized, double-blind, parallel-group, active controlled phase 3 study.
The study will comprise a single-blind, 2-week placebo run-in period followed by a randomized, double-blind, active controlled, 52-week treatment period followed by a 2-week follow-up period. Subjects will visit the clinic at Screening (Visit 1), at the end of the placebo run-in period (Visit 2/ Randomization), after 1, 3, 6, 9 and 12 months of double-blind treatment (Visit 3, 4, 5, 6 and 7) and 2
weeks after End of Trial (EoT), for a follow-up visit (Visit 8).

Intervention

Investigational Product and Dose:
* Combination of 5 mg solifenacin + 50 mg mirabegron

Comparative Drug and Dose:
* Solifenacin succinate 5 mg
* Mirabegron OCAS 50 mg

Study burden and risks

Based on the data available for the monotherapies and combination treatment, it is expected that the potential benefits of participating in the trial outweigh the risk.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

* Subject is male or female and at least 18 years of age;;* Subject is willing and able to complete the micturition diary and questionnaires correctly and able to measure his/her vital signs at home at stipulated time points, using the device provided by the study personnel, and to adequately record the readings;;* Subject has symptoms of *wet* OAB for at least three months

Exclusion criteria

* Subject has neurological cause for detrusor overactivity (e.g. neurogenic bladder, diabetic neuropathy with autonomic component or bladder involvement, or systemic or central neurological disease such as multiple sclerosis and Parkinson's disease with autonomic component or bladder involvement). An autonomic component can be inferred when autonomic functions are affected, including heart rate, blood pressure, perspiration and digestion.;* Subject has chronic inflammation such as bladder pain syndrome / interstitial cystitis, symptomatic bladder stones or any previous or current radiation cystitis.;* Subject has moderate to severe hepatic impairment;* Subject has severe renal impairment;* Subject has a clinically significant abnormal ECG;* Subject has a concurrent malignancy or history of cancer (except noninvasive skin cancer) within the last 5 years prior to screening.;* Subject has an average QTcF interval > 450 ms for males or > 470 ms for females based on the triplicate ECGs completed at Screening or is at risk of QT prolongation (e.g., family history of long QT syndrome, hypokalaemia).;* Subject has severe hypertension, which is defined as a sitting average systolic blood pressure * 180 mmHg and/or average diastolic blood pressure * 110 mmHg.;* In the opinion of the investigator the subject has clinically significant bladder outflow obstruction at risk of urinary retention;;* Subject has significant PVR volume (> 150 mL); ;* Subject has significant stress incontinence or mixed stress/urgency incontinence where stress is the predominant factor as determined by the investigator;;* Subject has an indwelling catheter or practices intermittent self-catheterization;;* Subject has evidence of urinary tract infection (UTI), chronic inflammation such as interstitial cystitis, bladder stones, previous pelvic radiation therapy or previous or current malignant disease of the pelvic organs;;* Subject has had intravesical treatment in the past 12 months with e.g., botulinum toxin, resiniferatoxin, capsaicin;

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-07-2014
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Betmiga
Generic name:	mirabegron
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vesicare
Generic name:	solifenacin succinate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	25-11-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	11-06-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	12-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-05-2016
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	EUCTR2012-005736-29-NL
CCMO	NL45587.018.13