Summary of Results for Laypersons

What as the Study Called?

An Open-label, Long-term, Multi-center Study to Assess the Safety and Efficacy of Fixed-dose Combinations of Solifenacin Succinate (6 mg and 9 mg) With Tamsulosin Hydrochloride OCAS 0.4 mg, in Male Subjects with Lower Urinary Tract Symptoms (LUTS) Associated With Benign Prostatic Hyperplasia (BPH) With a Substantial Storage Component. This study was also called the NEPTUNE II study.

Why was this Study Needed?

Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) is a common problem for men over 50 years old. BPH is a non-cancer enlargement of the prostate gland. LUTS include:

- Urinary storage symptoms like:
    - Having to empty the bladder more often than usual (called increased urinary frequency).
    - Sudden need to urinate which is difficult to delay (called urinary urgency).
    - Having a need to urinate at night (called nocturia).
- Problems emptying the bladder (called voiding symptoms) like:
    - A delay between trying to urinate and the stream actually beginning (called urinary hesitancy).
    - Having a weak urine stream.
    - A urine stream that stops and starts (called urinary intermittency).
    - Sensation of incomplete bladder emptying.
    - Dribbling.
    - Belly pain.

Voiding symptoms are more common than storage symptoms. However, storage symptoms are considered to be more bothersome. Storage symptoms can interfere with daily activities and impact quality of life.

The most common treatment for LUTS associated with BPH is medicines that work on the prostate. Alpha$_1$-adrenoceptor (AR) agonists is a type of medicine that works on the prostate. Tamsulosin is an alpha$_1$-AR agonist that is used to treat LUTS associated with BPH. This medicine helps reduce voiding symptoms but does not work very well on storage symptoms. This is because storage symptoms are caused by unwanted contraction of the muscles of the bladder. Storage symptoms are similar to those experienced by patients with an overactive bladder (OAB). OAB is commonly treated with medicines called antimuscarinics. Solifenacin succinate is an antimuscarinic medicine.

Researchers thought that using a fixed-dose combination (FDC) of an alpha$_1$-AR agonist and an antimuscarinic could lead to better control of voiding and storage symptoms. The alpha$_1$-AR agonist medicine selected was tamsulosin. The antimuscarinic medicine selected was solifenacin succinate.

This was an extension study of the 905-CL-055 study. Once patients completed the 12 week treatment period in study 905-CL-055 they were asked if they wanted to continue treatment by entering this study.

Study 905-CL-055 enrolled male patients with LUTS associated with BPH. The main question this study helped answer was if FDC treatment with tamsulosin and solifenacin succinate was better than tamsulosin alone to treat male patients with LUTS associated with BPH. Storage symptoms were a big problem for the patients enrolled in this study. The FDC tested was:

- FDC tamsulosin 0.4 mg and solifenacin 6 mg (called FDC 0.4 mg/6 mg)
- FDC tamsulosin 0.4 mg and solifenacin 9 mg (called FDC 0.4 mg/9 mg)

This extension study took place at 82 clinics in in Austria, Belgium, Belarus, Czech Republic, Germany, France, Hungry, Italy, The Netherlands, Poland, Russian Federation, Slovakia, and United Kingdom. The extension study started in April 2010 and ended in December 2011. The sponsor (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This was an extension study of the 905-CL-055 study. An extension study allows patients to continue receiving study medicines after a clinical study is completed. Once patients completed the 12 week treatment period in study 905-CL-055 they were asked if they wanted to continue receiving study medicines by entering study 905-CL-057.

Patients were assigned to 1 of 4 treatments in study 905-CL-055:

- Placebo
- Tamsulosin 0.4 mg alone
- FDC 0.4 mg/6 mg
- FDC 0.4 mg/9 mg

All patients enrolled in study 905-CL-057 started with 4 weeks of FDC tamsulosin/solifenacin 0.4 mg/6 mg treatment. After 4 weeks the patients returned to the clinic and subsequently returned 3 more times every 12 weeks. This study lasted 40 weeks. Patients were allowed to ask for a dose increase to FDC tamsulosin/solifenacin 0.4 mg/9 mg after 4 weeks of treatment at FDC tamsulosin/solifenacin 0.4mg/6 mg.

All patients had completed treatment in study 905-CL-055. The entry criteria for study 905-CL-057 were:

- Aged 45 years and older.
- Diagnosed with LUTS associated with BPH.
- Patients met very specific criteria which proved that they had experienced a lot of storage symptoms for 3 or more months.

A total of 1066 patients who completed study 905-CL-055 were enrolled in study 905-CL-057. A total of 1066 patients took at least 1 dose of study medicine under study 908-CL-057.

	Total (out of 1066 patients)
Age Group	
Aged 65 years or younger	540
Older than 65 years and younger than 75 years	417
Older than 75 years	109
Men	1066
Women	0
EU Countries	1028
Outside EU	38

What Were the Study Results?

FDC tamsulosin/solifenacin 0.4 mg/6 mg treatment was effective for the treatment of LUTS associated with BPH. Longer treatment resulted in better results.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called "adverse events" and are recorded whether or not they might be caused by the treatment taken. An "adverse reaction" is any medical problem or "adverse event" that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

The table below shows the most common adverse reactions experienced by patients while taking part in this study. Information from 1066 patients who received at least 1 dose of study medicine is included in the table below.

Adverse Reactions	**Group 1: Only FDC 0.4 mg/6 mg (out of 526 patients)**	**Group 2: FDC 0.4 mg/6 mg increased to 0.4 mg/9 mg (out of 132 patients)**	**Group 3: Other dose sequences (out of 408 patients)**	**Total (out of 1066 patients)**
Dry mouth	55	12	64	131
Constipation	20	3	28	51
Heartburn	9	1	7	17
Feces hard	4	0	6	10
Urinary hesitation	8	0	2	10
Increased urine left in the bladder after urinating	6	0	3	9

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Adverse Reactions	Group 1: Only FDC 0.4 mg/6 mg (out of 526 patients)	Group 2: FDC 0.4 mg/6 mg increased to 0.4 mg/9 mg (out of 132 patients)	Group 3: Other dose sequences (out of 408 patients)	Total (out of 1066 patients)
Ejaculation of semen backward toward the bladder instead of forward through the urethra	1	1	5	7
Painful urination	2	0	4	6
Impotence or the inability to have or maintain an erection during sexual intercourse	1	1	4	6

Group 1: the group of patients who received only the FDC 0.4 mg/6 mg and in Study 905-CL-055 did not receive FDC 0.4 mg/9 mg

Group 2: the group of patients who received the FDC 0.4 mg/6 mg during the first 4 weeks increased to 0.4 mg/9 mg thereafter and in Study 905-CL-055 did not receive the FDC 0.4 mg/6 mg

Group 3: All other dose sequences not included in Group 1 and Group 2

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. Some patients had serious adverse reactions: 7 patients in the FDC tamsulosin/solifenacin 0.4 mg/6 mg treatment group and 5 patients in the FDC tamsulosin/solifenacin 0.4 mg/9 mg treatment group.

Three patients died during the study. The patients did not die because of study medicine.

Where Can I Learn More About This Study?

Astellas might perform additional trials to better understand FDC tamsulosin/solifenacin succinate treatment.

This summary of the clinical study results is available online at http://www.astellasclinicalstudyresults.com. Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. If you have questions about FDC tamsulosin/solifenacin succinate treatment, please discuss these with your doctor.

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