Summary of Results for Laypersons

What was the Study Called?

A Study to Evaluate the Overall Effect of Solifenacin 5 mg and 10 mg on Bladder Wall Thickness and Urinary Nerve Growth Factor in Female Subjects with Overactive Bladder and a Diagnosis of Detrusor Overactivity – A Double-blind, Randomized, Placebo-controlled, Parallel-group, Multi-center Study. This is also known as the SHRINK study.

Why was this Study Needed?

People with overactive bladder have symptoms such as:

- Sudden need to urinate which is difficult to delay (called urinary urgency).
- Having to empty the bladder more often than usual (called increased urinary frequency).
- Any loss of urine due to not being able to control when to empty the bladder (called urinary incontinence).

There are medicines for adults with overactive bladder. These include solifenacin succinate (also known as YM905 and VESIcare®).

The thickness of the bladder wall could be an indicator of overactive bladder. A natural chemical is passed into the urine (called urinary nerve growth factor). The level of this chemical could also be an indicator. This study tested solifenacin succinate (5 mg and 10 mg) and placebo. It helped answer what the effect of the study medicines was on the possible indicators. The study also helped answer if the possible indicators were linked to the bladder symptoms.

This study took place at 79 clinics in Austria, Belgium, Bulgaria, Canada, Czech Republic, France, Germany, Hungary, Israel, Italy, Norway, Poland, Romania, Russian Federation, Slovakia, Spain, Sweden, Turkey, the UK and the US. The study took place from January 2010 to June 2011. When the study ended, 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 a "blinded" study. In this study, the patients and the researchers did not know who took which of the medicines (solifenacin succinate 5 mg and 10 mg or placebo). A "placebo" is a dummy treatment such as a tablet or capsule that looks like a medicine, but does not have any medicine in it. Using a placebo helps make study results fair and unbiased, because researchers and patients cannot tell who is taking a placebo, and who is taking the test medicine.

Women over 18 years old could take part in the study if:

- They had bladder problems for at least 3 months.
- They had involuntary contractions of the bladder muscle.
- The amount of urine left in their bladder after urination was less than 50 mL.

- They had not taken antimuscarinic treatment for 6 months before visit 1.

Patients could not take part in this study if:

- They leaked urine under stress conditions (exercise, laughing). Or their bladder muscle did not work well.
- They had infections of the structures that carry urine or a significant obstruction of the bladder outlet.
- They had a surgery of the structures that carry urine within 6 months before starting the study.
- They had catheters (tube for draining urine) inserted in their bladders.
- They had radiation therapy in the lower abdomen.

The study had 4 visits. At visit 1, patients were checked to see if they could be in the study. The patients then started a 2-week "run-in period." Patients took placebo once daily for 2 weeks. Patients also kept a diary of their bladder symptoms. At visit 2, the diaries were checked to see if patients could remain in the study.

Patients who could remain in the study were picked for 1 of the following 3 study treatments by chance alone:

- 5 mg of solifenacin succinate once daily,
- 10 mg of solifenacin succinate once daily or
- placebo once daily.

Patients took study medicine for up to 12 weeks. The patients returned to the clinic for a check-up every 6 weeks (visits 3 and 4).

A total of 599 patients were in the study. A total of 547 patients took at least 1dose of study medicine. Patients took the following treatments:

- 183 patients took solifenacin succinate 5 mg once daily,
- 178 patients took solifenacin succinate 10 mg once daily and
- 186 patients took placebo once daily.

543 of these patients had data available after the first dose of study medicine. They are included in the table below.

	Number of Patients (out of 543 patients)
Age Group	
Aged less than18 years	0
Aged 18 years and older	543
Aged between 18 and 64 years	unknown
Aged 65 years and older	unknown
Clinic Location	
EU Countries	352
Austria	3
Belgium	12
Bulgaria	47
Czech Republic	25
France	13
Germany	10
Hungary	23
Italy	27
Poland	98
Romania	1
Slovakia	35
Spain	34
Sweden	12
The UK	12
Outside EU	191

What Were the Study Results?

The thickness of the bladder wall could be an indicator of overactive bladder. The level of a natural chemical (called urinary nerve growth factor) could also be an indicator. The results of the study showed that the study medicines had no clear effect on these indicators. It did not matter if patients took solifenacin succinate 5 or 10 mg once daily. The study found no clear link between how bad the bladder symptoms were and the thickness of the bladder wall. There was also no clear link between the bladder symptoms and the level of a natural chemical (called urinary nerve growth factor).

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.

Data were available for 543 patients after they took the first dose of study medicine. The table below shows the most common adverse reactions experienced by these patients.

Adverse Reactions	Placebo (out of 186 patients)	Solifenacin Succinate 5 mg (out of 182 patients)	Solifenacin Succinate 10 mg (out of 175 patients)	Total (out of 543 patients)
Dry mouth	2 (1.1%)	16 (8.8%)	30 (17.1%)	48 (8.8%)
Constipation	6 (3.2%)	8 (4.4%)	9 (5.1%)	23 (4.2%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. Two patients had serious adverse reactions. Both patients were in the solifenacin succinate 10 mg group.

One patient died during the study. The death was not because of the study medicine.

Where Can I Learn More About This Study?

Astellas might perform additional trials to better understand solifenacin succinate.

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 solifenacin succinate, please discuss these with your doctor.

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