Summary of Results for Laypersons

What was the Study Called?

A Phase 3, Double-blind, Randomized, Multicenter, Placebo-controlled Sequential Dose Titration Study to Assess Efficacy, Safety and Population Pharmacokinetics of Solifenacin Succinate Suspension in Pediatric Subjects from 5 to less than 18 Years of Age with Overactive Bladder

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®). It comes in tablets. Tablets can be difficult to swallow for children. A liquid form of solifenacin succinate was made for children to take by mouth.

This study tested the liquid form (called solifenacin succinate suspension) in children and teenagers with overactive bladder. This study helped answer if bladder function in these patients was improved more by the liquid form than by placebo. It was also important to find out what unwanted effects these patients had from the study medicine. The study measured the level of solifenacin succinate in the blood of the patients who took the liquid form.

This study took place at 50 clinics in Belgium, Brazil, Canada, Denmark, Mexico, Norway, Philippines, Poland, Serbia, South Africa, South Korea, Sweden, Turkey, the UK, Ukraine and the US. The study took place from June 2012 to January 2014. 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. The patients and the researchers did not know who took solifenacin succinate suspension or placebo. A "placebo" is a dummy treatment that looks like the solifenacin succinate suspension, 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.

Children and teenagers with bladder problems could take part in the study if:

- The children were 5 to 11 years old and the teenagers were 12 to 17 years old.
- The patients had a normal weight and height for their age.
- Female patients were not pregnant.
- Patients who were having sex used reliable birth control methods.

Patient could not take part in this study if:

- They had to urinate less than 5 times during the day.
- They had to urinate at least once every hour during the day. The amount of urine was less than 50% of what their bladder could hold. They urinated normally during the night.
- The cause of their bladder problems was not overactive bladder.
- They had bedwetting problems.
- They urinated an excessive amount (more than 75 mL per kg of body weight over 24 hours).

The study had 8 visits. At visit 1, patients were checked to see if they could be in the study. Patients received counseling for their bladder problems from visit 1 until the end of the study. Patients who were taking medicine for their bladder problems went off their medicine for 2 weeks. At visit 2, patients 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 3, the diaries were checked to see if patients could remain in the study. Patients could remain in the study if their diaries showed that:

- Patients had daytime wetting on at least 4 occasions during a 7-day period.
- The maximum amount of their urine (not counting morning urine) was not more 390 mL.
- The amount of urine left in their bladder after urination was 20 mL or less.

Patients who could remain in the study were picked for 1 of the study treatments by chance alone. These once daily treatments were solifenacin succinate suspension (dose "5") or placebo. At visits 4, 5 and 6, the dose of solifenacin succinate suspension could be changed to determine the best dose for each patient. The possible doses of solifenacin succinate suspension were:

- Dose "2.5," which was comparable to 2.5 mg of solifenacin succinate tablets taken once daily in adults,
- Dose "5," which was comparable to 5 mg of solifenacin succinate tablets taken once daily in adults,
- Dose "7.5," which was comparable to 7.5 mg of solifenacin succinate tablets taken once daily in adults, and
- Dose "10," which was comparable to 10 mg of solifenacin succinate tablets taken once daily in adults.

After visit 6, patients took the same dose of study medicine for 3 weeks. At visit 7, patients took their last dose of study medicine. Visit 8 was 2 to 3 days later. At visits 7 and 8, blood samples were taken. Patients kept a diary of their bladder symptoms for 7 days before each clinic visit.

A total of 148 children and 41 teenagers were in the study. A total of 146 children and 41 teenagers took study medicine for up to 12 weeks in this study. Patients took 1 of the following treatments once daily:

- 73 children took placebo.
- 73 children took solifenacin succinate suspension.

- 19 teenagers took placebo.
- 22 teenagers took solifenacin succinate suspension.

	Number of Children (out of 146 patients)	Number of Teenagers (out of 41 patients)
Age Group		
Aged 5 to less than 12 years	146	0
Aged 12 to less than 18 years	0	41
Gender		
Girls	79	33
Boys	67	8
Clinic Location		
EU	83	10
Belgium	34	4
Denmark	19	3
Poland	20	2
Sweden	8	1
The UK	2	0
Outside EU	63	31

What Were the Study Results?

This study tested the liquid form (called solifenacin succinate suspension) in children and teenagers with overactive bladder. These patients took the liquid form or placebo. Study results showed that in children the liquid form improved bladder function more than did placebo.

This study measured the level of solifenacin succinate in the blood of the patients who took the liquid form. Blood levels in most patients were comparable to what was seen in the past in adults with overactive bladder. There was no difference in blood levels between children and teenagers.

The study showed that children and teenagers with overactive bladder who took the liquid form did not have a lot of unwanted effects.

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 who took at least 1 dose of study medicine. More children in the solifenacin succinate suspension groups than in the placebo group had constipation. And more children in the solifenacin succinate suspension groups than in the placebo group had abnormal electrical conduction

within the heart. Abnormal electrical conduction within the heart was not common in teenagers. Teenagers did not have constipation.

	Number of Children		Number of Teenagers	
Adverse Reaction	**Placebo (out of 73 patients)**	**Solifenacin Succinate Suspension (out of 73 patients)**	**Placebo (out of 19 patients)**	**Solifenacin Succinate Suspension (out of 22 patients)**
Constipation	2 (2.7%)	4 (5.5%)	0	0
Abnormal electrical conduction within the heart	2 (2.7%)	4 (5.5%)	1 (5.3%)	1 (4.5%)
Dry mouth	1 (1.4%)	2 (2.7%)	1 (5.3%)	0

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. One patient had a serious adverse reaction. This patient was a child who took placebo.

None of the patients died during the study.

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.

Sponsor contact details:

Astellas Pharma Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands