Summary of Results for Laypersons

What was the Study Called?

A Phase 3, Open-label, Baseline-controlled, Multi-center, Sequential Dose-titration Study to Assess the Pharmacokinetics, Long-term Efficacy and Safety of Solifenacin Succinate Suspension in Children from 6 Months to less than 5 Years of Age with Neurogenic Detrusor Overactivity

Why was this Study Needed?

Neurogenic detrusor overactivity (called NDO) describes a problem where bladder control is poor due to problems with nerves to the bladder. The condition is different from overactive bladder. People with overactive bladder have symptoms such as a sudden need to urinate which is difficult to delay; having to empty the bladder more often than usual; or any loss of urine due to not being able to control when to empty the bladder.

NDO can be found frequently in conditions called spina bifida (SB) and cerebral palsy (CP). In SB the bones and nerves of the spine, and sometimes the brain, do not form correctly. In CP the nerves and brain develop correctly but are permanently damaged usually at the time of birth. Both SB and CP can cause the permanent nerve wiring problems that disturb bladder function – called NDO. Patients with NDO may benefit from medicines that improve bladder function.

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 (called solifenacin succinate oral suspension) was made for children to take by mouth.

This study tested the liquid form of solifenacin in children with NDO. This study looked at how much urine the bladder can hold before urine starts to leak or the patient feels pain or discomfort. This is called the maximum bladder capacity. This study helped find out how much a 24-week treatment with solifenacin can improve the maximum bladder capacity of these patients. It was also important to find out what unwanted effects these patients had from solifenacin.

This study took place at 8 clinics in Belgium, the Philippines, Poland, South Korea, the UK and the US. The study took place from September 2013 to December 2015. 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 an "open-label" study. What this means is that all patients knew that they took solifenacin succinate oral suspension.

Children with NDO could take part in the study if:

- The children were 6 months to less than 5 years old.

- They weighed at least 6 kg.
- Their bones and nerves of the spine did not form correctly.
- A doctor had determined that they had NDO.
- They had detrusor sphincter dyssynergia (called DSD). The sphincter is the muscle that works like a tap to open or close the tube (urethra) that drains the bladder. DSD is a particular problem, often caused by NDO, where the nerves that help synchronization of the bladder and the sphincter are damaged. This causes a buildup of pressure in the bladder.
- They used a clean tube (catheter) to help empty their bladder. They used this catheter (putting it in and taking it out) to empty the bladder several times a day.
- The study doctor thought that they were capable of emptying their bladder with a catheter 4 to 6 times a day. The study doctor thought that they could do that for the duration of the study.
- They were able to swallow the study medicine.

Children with NDO could not take part in this study if:

- Their bladder could hold less than 25% of what was expected based on their age.
- The urine in their bladder flowed backwards into the ureters (the tube between the kidney and the bladder) and kidneys. And this condition was severe.
- They had poor bladder control that was not related to their NDO.
- They had a catheter that was left continuously inserted into their bladders. They did so within 4 weeks before visit 2, which is when patients took their first dose of study medicine.
- They had a surgery to enlarge their bladders.
- They had a surgery to improve the activity of the sphincter.

The study had 9 visits. At visit 1, patients were checked to see if they could be in the study. Patients who were taking medicine for their bladder problems went off their medicine. The parents or legal guardian of the patients kept a diary of the patient's bladder symptoms. They did this for 3 days before visits 2 through 9. At visit 2, the patients were checked to see if they could remain in the study. Patients who could remain in the study took their first dose of the liquid form of solifenacin. Depending on when the patients started in the study, their first dose was "5" or "2.5." Dose "5" was comparable to 5 mg of solifenacin succinate tablets taken once daily in adults. Dose "2.5" was comparable to 2.5 mg of solifenacin succinate tablets taken once daily in adults. Patients who were younger than 2 years received their first dose at visit 2. After dosing, they stayed at the clinic for 5 hours to check for safety issues. Patients who were 2 years or older took their first dose at home the day after visit 2.

Patients returned to the clinic every 3 weeks for visits 3 through 6. At these visits, the dose of solifenacin could be changed to determine the best dose for each patient. Patients younger than 2 years who received an increased dose stayed at the clinic for 5 hours to check for safety issues. At visit 6, a blood sample was taken. The possible doses of the liquid form of study medicine 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 remained on the same dose of study medicine for 40 weeks. Patients returned to the clinic every 12 weeks for a check-up and a blood sample (visits 7 and 8). The last visit was at week 52.

A total of 23 children were in the study and took at least 1 dose of study medicine.

	Number of Children (out of 23 patients)
Age Group	
Aged 6 months to less than 2 years	4
Aged 2 to less than 5 years	19
Gender	
Girls	14
Boys	9
Clinic Location	
EU	11
Belgium	1
Poland	9
UK	1
Outside EU	12
Philippines	6
South Korea	5
US	1

What Were the Study Results?

This study tested the liquid form of solifenacin in children with NDO. This study looked at the effect of solifenacin on the maximum bladder capacity of these patients. At study start, the maximum bladder capacity was 92.3 mL on average. It increased by 37.0 mL on average after 24 weeks of treatment with solifenacin.

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.

Five patients who took at least 1 dose of study medicine each had 1 or more adverse reactions. The table below shows the most common adverse reactions experienced by these

patients. Three patients had constipation and 2 patients had dry mouth. These adverse reactions are expected with the use of solifenacin. Adults who took this study medicine also had these adverse reactions.

Adverse Reaction	Solifenacin Succinate Suspension (out of 23 patients)
Any adverse reaction	5 (21.7%)
Constipation	3 (13.0%)
Dry mouth	2 (8.7%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. None of the patients had a serious adverse reaction.

Where Can I Learn More About This Study?

This document reflects the information available as of August 2017.

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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