Summary of Results for Laypersons

What was the Study Called?

A Phase 3, Open-label, Baseline-controlled, Multicenter, Sequential Dose Titration Study to Assess the Long-term Efficacy and Safety, and the Pharmacokinetics of Solifenacin Succinate Suspension in Patients from 5 to Less than 18 years of Age with Neurogenic Detrusor Overactivity (NDO). This is also known as the MONKEY study.

Why was this Study Needed?

People with neurogenic detrusor overactivity (called NDO) have permanent problems with the wiring of the nerves to the bladder. People with spina bifida or cerebral palsy often have NDO. In spina bifida, the bones and nerves of the spine, and sometimes the brain, do not form correctly. In cerebral palsy, the nerves and brain develop correctly but are permanently damaged usually at the time of birth. Because of their nerve wiring problems, people with NDO have symptoms related to bowel function and mobility. They have problems emptying their bladder. They often need to use a clean tube (catheter) to help empty their bladder. Medicines may help people with NDO keep their bladder healthy and prevent damage to their kidneys.

There are medicines for adults with bladder problems. 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 suspension) was made to be easier to swallow by children.

This study tested the liquid form of solifenacin in children and teenagers 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 20 clinics in Belgium, Brazil, Denmark, Mexico, the Philippines, Poland, South Korea, Turkey and the US. The study took place from August 2012 to April 2016. 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. All patients knew that they took solifenacin succinate suspension.

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

- They were 5 to less than 18 years old.
- A doctor had determined that they had NDO. They had involuntary contractions of their bladder muscle, which led to an increase in bladder pressure. The increase was bigger

than what is seen in healthy children. The increase was noted at study visit 3, when patients were to take their first dose of study medicine.
- They used a 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 determined that they were capable of emptying their bladder with a catheter 4 to 6 times a day. The study doctor believed that they could do that for the duration of the study.
- They took medicines for their NDO for at least 6 months before study start. These medicines were the same type as solifenacin.
- They had a normal weight for their age.

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

- They were pregnant or were breastfeeding their baby.
- They had a condition that might cause loss of urine due to not being able to control when to empty the bladder. This condition was different from their NDO.
- They had a surgery to enlarge their bladders.
- Their bladder could hold less than 25% of what was expected based on their age.
- They had a treatment that used electrical stimulation to treat muscle spasms and pain.
- The urine in their bladder flowed backwards into the ureters (the tube between the kidney and the bladder) and kidneys. This problem was severe.

The study had 10 visits. At visit 1, patients were checked to see if they could be in the study. The parents or legal guardian of the patients kept a diary of the patient's bladder symptoms. They did this for 7 days before visits 2 through 10. At visit 2, patients who were taking medicine for their bladder problems went off their medicine. Two weeks later, they returned to the clinic for visit 3. At visit 3, 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. Their first dose was comparable to 5 mg of solifenacin succinate tablets taken once daily in adults.

Patients returned to the clinic every 3 weeks for visits 3 through 7. At these visits, the dose of solifenacin could be changed to determine the best dose for each patient. At visit 7, 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 the best dose of study medicine for a patient was determined, the patient remained on that dose for at least 40 weeks. Patients returned to the clinic every 12 weeks for a check-up and a blood sample (visits 8 and 9). The last visit (visit 10) was at week 52.

A total of 42 children and 34 teenagers were in the study. They took at least 1 dose of study medicine.

	Number of Children (out of 76 patients)
Age Group	
Aged 5 to less than 12 years	42
Aged 12 to less than 18 years	34
Gender	
Boys	37
Girls	39
Clinic Location	
EU	33
Belgium	6
Denmark	3
Poland	24
Outside EU	43
Brazil	7
Mexico	3
The Philippines	16
South Korea	6
Turkey	7
The US	4

What Were the Study Results?

This study tested the liquid form of solifenacin in children and teenagers with NDO. This study looked if solifenacin could improve their maximum bladder capacity or how full their bladder could get safely. After 24 weeks of solifenacin, the average increase of the maximum bladder capacity was 57.2 mL. This is a useful increase in bladder size.

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. Three patients had abnormal electrical conduction within the heart. Doctors do not consider this to be an important or dangerous finding. Six patients had constipation. Constipation is expected with the use of solifenacin. Adults who took this study medicine also had constipation. Most of the time, constipation is easy to treat with laxatives.

Adverse Reaction	Solifenacin Succinate Suspension (out of 76 patients)
Constipation	6 (7.9%)
Abnormal electrical conduction within the heart	3 (3.9%)

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.

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.

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