Summary of Results for Laypersons

Astellas is grateful to the young patients who took part in this clinical study. Thank you.

What was the Study Called?

An Open-label, Phase 3 Study with Mirabegron in Children from 3 to less than 18 Years of Age with Neurogenic Detrusor Overactivity (NDO). This is also known as the Crocodile study.

Why was this Study Needed?

People with neurogenic detrusor overactivity (or NDO for short) have poor bladder control because of permanent problems with the wiring of the nerves to the bladder. They can have periods of high pressure in their bladder. This can be dangerous for the kidneys. It can also cause other problems like losing urine involuntarily (this is called incontinence). People with neurogenic detrusor overactivity (NDO) often need to use a clean tube (catheter) to help empty their bladder. There are standard treatments for children with NDO but they may not work in all children. And they may have unwanted effects. There was a need to find new medicines for children with neurogenic detrusor overactivity (NDO).

This study looked at how well mirabegron worked in treating children and adolescents with neurogenic detrusor overactivity (NDO). To do this, the study measured how much urine the bladder can hold before urine starts to leak or the child feels pain or discomfort. This is called the maximum bladder capacity. This study compared the change in maximum bladder capacity after children took study medicine for 24 weeks. It was also important to find out what unwanted effects the children had from the study medicine.

The study started in June 2016 and ended in May 2019. When the study ended, the sponsor of this study (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. That means that each patient, the parents of each patient and the study doctors knew which study medicine that patient took.

This study was open to young patients with neurogenic detrusor overactivity (NDO) aged 3 to less than 18 years. They needed medicine to treat their neurogenic detrusor overactivity (NDO). They weighed at least 11 kg. They used a catheter. A catheter is a clean tube used for emptying the bladder several times a day. They had been doing this for at least 4 weeks before the start of the study.

During the study, the study doctor did a check-up of the children at several study visits. At the first visit, the children were checked to see if they could be in the study. Children who could be in the study completed (or a parent completed) a 7-day electronic diary (e-diary). The child (or parent) measured the volumes of urine obtained from the catheter. And they recorded it in the e-diary. If a child was taking medicines for their neurogenic detrusor

overactivity (NDO), they stopped them for 2 weeks. This allowed the medicine to leave their body.

The children who could remain in the study took mirabegron once a day for 24 to 52 weeks. The first 24 weeks, researchers looked at how well the medicine worked to increase the maximum bladder capacity. The next 28 weeks, researchers looked at the long term safety of the medicine. Mirabegron comes in tablets. Children with a body weight of 35 kg or more took mirabegron tablets (25 mg or 50 mg) based on their weight. Tablets can be difficult to swallow for some children. For this study, loose mirabegron was stirred into water (called a suspension). This suspension was easier for children to swallow. Children with a body weight less than 35 kg took mirabegron suspension (8 mg/mL), based on their weight. Any child who could not swallow a tablet could take mirabegron suspension.

This study took place at 32 clinics in several countries. 91 children were in the study. Out of these, 86 children took at least 1 dose of study medicine.

	Number of Children
Age Group	
Aged 3 years to less than 12 years	55
Aged 12 years to less than 18 years	31
Sex	
Boys	39
Girls	47
Clinic Location	
European Union Countries (*at the time of the study*)	43
Belgium	2
Croatia	7
Denmark	2
Latvia	2
Lithuania	7
Poland	15
Romania	6
Slovakia	2
Outside European Union	43
Australia	1
Israel	1
Jordan	3
Malaysia	3
Mexico	3
Norway	5
Philippines	10
Serbia	4
South Korea	6
Taiwan	1
Turkey	6

What Were the Study Results?

An increase in the amount of urine the bladder can hold is an improvement.

The maximum bladder capacity increased in both age groups after 24 weeks of study medicine. Statistical tests showed that the increase was not likely to be due to chance.

Average Increase in Maximum Bladder Capacity		
Children (3 to less than 12 years)	**Adolescents (12 to less than 18 years)**	**All Patients (3 to less than 18 years)**
72.09 mL	113.21 mL	87.20 mL

In this study, mirabegron was effective in patients aged 3 to less than 18 years with neurogenic detrusor overactivity (NDO).

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.

14 children and adolescents (16.3%, 14 out of 86 children and adolescents) had adverse reactions during the study.

The table below shows the most common adverse reactions experienced by children and adolescents who took at least 1 dose of study medicine in this study.

Adverse Reaction	**Number of Patients (out of 86 children and adolescents)**
Urinary Tract Infection caused by bacteria	3 (3.5%)
Constipation	2 (2.3%)
Nausea or the urge to vomit	2 (2.3%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care.

None of the children experienced serious adverse reactions in this study.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study. You can find this summary and more information about this study 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. This summary only shows

the results of this 1 study. Your child's doctor may help you understand more about the results of this study.

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