Summary of Results for Laypersons

What was the Study Called?

A Multicentre, Open-label, Single Ascending Dose Phase 1 Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Mirabegron OCAS Tablets in Pediatric Subjects from 5 to Less than 18 Years of Age with Neurogenic Detrusor Overactivity (NDO) or Overactive Bladder (OAB)

Why was this Study Needed?

People with overactive bladder problems have symptoms such as:

- Sudden need to urinate which is difficult to delay (called urinary urgency).
- Having to empty the bladder more than usual (called increased urinary frequency).
- Not being able to control when to empty the bladder (called urgency incontinence).

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.

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.

There are medicines for adults with overactive bladder. These include mirabegron (also known as Betmiga®, Myrbetriq® and Betanis®). It comes in tablets. It is not approved to treat NDO.

This study tested mirabegron in children and teenagers with NDO or overactive bladder. The study helped answer how well mirabegron is absorbed into the body and how long it stays in the body. It was also important to find out what unwanted effects patients had from mirabegron. This study was not designed to test whether mirabegron was useful or effective.

This study took place at 9 clinics in Belgium, Denmark, Norway and Poland. The study took place from September 2014 to September 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. All patients knew that they took a single dose of mirabegron.

This was also a “dose escalation” study. Patients were treated in groups. Group 1 was teenagers who took a low dose after breakfast. These patients were evaluated. If no safety issues were seen, then group 2 (children) took a low dose after breakfast. Also, group 3 (teenagers) took a high dose after breakfast. Group 2 was evaluated. If no safety issues were

seen, then group 4 (children) took a high dose after breakfast. Group 4 was evaluated. If no safety issues were seen, then group 5 (children) took a high dose without breakfast. The low and high doses were based on body weight.

Low dose

- 25 mg of mirabegron for patients who weighed between 20.0 and less than 55.0 kg.
- 50 mg of mirabegron for patients who weighed at least 55.0 kg.

High dose

- 50 mg of mirabegron for patients who weighed between 20.0 and less than 40.0 kg.
- 75 mg of mirabegron for patients who weighed at least 40.0 kg.

Children and teenagers could take part in the study if:

- The children were 5 to less than 12 years old and the teenagers were 12 to less than 18 years old.
- A doctor had determined that they had NDO or overactive bladder.
- They weighed at least 20.0 kg. Patients with overactive bladder had a normal weight and height for their age. Patients with NDO were not extremely overweight and were not underweight.
- They could swallow the study medicine.
- Patients who were having sex used reliable birth control methods.

Patients could not take part in this study if:

- Female patients were pregnant.
- They had, or had in the past, abnormal electrical conduction within the heart. Or they were at risk for this; for example, they had a decreased blood level of potassium or a family member had abnormal electrical conduction of the heart.
- They had an abnormal pulse rate.
- They had high blood pressure.
- The study doctor thought that the patients were too sick to be in the study.

The study had 5 visits. At the first visit patients were checked to see if they could be in the study. Patients who could be in the study went off their medicines. Their heart rate was measured for 24 hours by using a medical device (Holter). This was done within 4 days before the treatment day. Patients arrived at the clinic on the morning of the treatment day (day 1). The study doctor started a 24-hour heart rate measurement (Holter) for all patients. Patients in groups 1 to 4 had not eaten breakfast at home and ate a light breakfast at the clinic. These patients took a low or high dose of mirabegron within 1 hour after breakfast. Patients in group 5 took a high dose of mirabegron. They had fasted from at least midnight before they took study medicine. They remained fasted until 4 hours after they took study medicine. Then the patients in group 5 ate a light lunch. Blood samples were taken from all patients after they took study medicine. Patients returned to the clinic for blood samples on day 2 and on 2 other days between days 3 and 7.

A total of 42 patients were in this study. A total of 34 patients took study medicine.

	Number of Patients (out of 34 patients)
Age Group	
Aged 5 to less than 12 years	19
Aged 12 to less than 18 years	15
Gender	
Girls	23
Boys	11
Clinic Location	
EU Countries	26
Belgium	1
Denmark	11
Poland	14
Outside EU	8
Norway	8

What Were the Study Results?

This study was conducted in children and teenagers with NDO or overactive bladder. The study looked at how well mirabegron was absorbed into the body and how long it stayed in the body. The study showed that levels of mirabegron in blood depended on the dose, age and food state in each group. The doses in this study led to mirabegron blood levels that are known to be effective in adults.

Children and teenagers with NDO or overactive bladder who took mirabegron did not have a lot of unwanted effects. The dose they took was up to 75 mg.

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.

One patient (out of 34 patients) had an adverse reaction. The patient had abnormal electrical conduction within the heart.

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 may perform additional studies to better understand mirabegron.

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 mirabegron, please discuss these with your doctor.

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