Summary of Results for Laypersons

What was the Study Called?

Safety and Efficacy of Mirabegron as Add-on Therapy in Patients with Overactive Bladder Treated with Solifenacin: A Postmarketing Open-label Study in Japan

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 than usual (called increased urinary frequency).
- Not being able to control when to empty the bladder (called urgency incontinence).

There are several medicines for overactive bladder in adults. They include solifenacin and mirabegron.

The patients in this study used to take solifenacin on its own for their bladder problems. In this study they also took mirabegron. The study helped answer whether mirabegron helped treat the bladder problems in these patients when added to solifenacin treatment. It was also important to find out what unwanted effects these patients had from mirabegron.

This study for mirabegron (also known by its brand names Betmiga®, Myrbetriq® and Betanis®) took place at 29 clinics in Japan. The study took place from October 2012 to July 2013. 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 and mirabegron.

The dose of solifenacin was 2.5 or 5 mg once daily. The dose of mirabegron was 25 mg once daily. Some patients took 50 mg mirabegron once daily later in the study.

Men and women could take part in the study if:

- They were 20 years or older.
- They had bladder problems.
- They took 2.5 or 5 mg solifenacin once daily for at least 4 weeks before starting the study.
- They could walk to the bathroom without help.
- They had a specified minimum score on a questionnaire about their bladder problems.

Patients could not take part in this study if:

- They did not have urgency incontinence.
- They leaked urine under stress conditions (exercise, laughing).
- They did not have bladder problems all the time.

- They had infections of the structures that carry urine or a significant obstruction of the bladder outlet.
- They had bladder cancer or prostate cancer or they had those cancers in the past.

The study had 6 visits. At visit 1 patients were checked to see if they could be in the study. Patients who could be in the study took solifenacin for 2 weeks. The daily dose of solifenacin was the same as before starting the study. At visit 2 patients returned to the clinic. Their scores on a questionnaire about their bladder problems were checked to see if the patients could remain in the study. Patients who could remain in the study took 25 mg mirabegron once daily. They also took the same dose of solifenacin as before. The patients returned to the clinic for a check-up every 4 weeks (visits 3 through 6). After 8 weeks (visit 4) the study doctor checked if the 25 mg mirabegron helped the bladder problems. If the bladder problems were still the same, then patients took 50 mg mirabegron once daily. They continued to take the same dose of solifenacin as before. Patients took study medicines for up to 16 weeks.

A total of 281 patients were in this study. A total of 280 patients took solifenacin for the first 2 weeks. A total of 223 patients took both solifenacin and mirabegron for up to 16 weeks. Patients took 1 of the following treatments once per day:

- 35 patients took both 2.5 mg solifenacin and 25 mg mirabegron.
- 37 patients took both 2.5 mg solifenacin and 50 mg mirabegron.
- 58 patients took both 5 mg solifenacin and 25 mg mirabegron.
- 93 patients took both 5 mg solifenacin and 50 mg mirabegron.

	Number of Patients (out of 223 patients)
Age Group	
Aged between 18 and 64 years	101
Aged 65 years and older	122
Gender	
Men	37
Women	186
Clinic Location	
EU Countries	0
Outside EU	223

What Were the Study Results?

The patients in this study used to take solifenacin on its own for their bladder problems. In this study they also took mirabegron. The study showed that when patients took both study medicines, their bladder problem symptoms improved.

Patients with bladder problems who took both study medicines did not have a lot of unwanted effects. Their dose of solifenacin was 2.5 or 5 mg. Their dose of mirabegron was 25 or 50 mg. They took the study medicines once daily for up to 16 weeks.

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 reaction experienced by patients who took at least 1 dose of study medicine during the study. More patients who took 5 mg solifenacin and 25 mg mirabegron had constipation compared to the other patients.

	Number of Patients Who Took 2.5 mg Solifenacin		Number of Patients Who Took 5 mg Solifenacin		
Adverse Reaction	**25 mg Mirabegron (out of 35 patients)**	**50 mg Mirabegron (out of 37 patients)**	**25 mg Mirabegron (out of 58 patients)**	**50 mg Mirabegron (out of 93 patients)**	**Total (out of 223 patients)**
Constipation	2 (5.7%)	2 (5.4%)	5 (8.6%)	5 (5.4%)	14 (6.3%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. One patient experienced a serious adverse reaction. The patient took 5 mg solifenacin and 25 mg mirabegron.

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.

Sponsor contact details:

Astellas Pharma Inc.
2-5-1, Nihonbashi-Honcho
Chuo-ku
Tokyo 103-8411
Japan