Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-Blind, Parallel Group, Placebo and Active Controlled, Multicenter Study to Assess the Efficacy and Safety of Mirabegron in Subjects with Symptoms of Overactive Bladder. This study is also known as the SCORPIO study.

Why was this Study Needed?

People suffering from overactive bladder problems, with symptoms such as increased number of times they urinate and feeling quicker the need to urinate, with or without episodes of leaking before reaching the toilet may benefit from medicines. Medicines are already available, but some of them may cause unwanted effects and some do not work in all patients.

This study was done to find out how well mirabegron treats these bladder problems. Mirabegron is a prescription medicine used to treat the symptoms such as:

- Suddenly needing to urinate (called 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).

The main question this study helped answer was if mirabegron was better than placebo in reducing the number of leaking or wetting accidents per day and reducing the number of times patients urinated per day. Also, it was important to find out what unwanted effects mirabegron might cause and to look at how well mirabegron might work in comparison with another medicine used to treat bladder problems (tolterodine).

This study for mirabegron (also known by its brand names Betmiga ®, Myrbetriq ®, Betanis ®) took place at 189 clinics in 26 countries in Europe and Australia between April 2008 and March 2009. 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 a “blinded” study. In this study, the patients and the researchers did not know who took which of the treatments (mirabegron, tolterodine, or placebo).

A “placebo” is a dummy treatment such as a tablet or capsule that looks like a medicine, but does not have any medicine in it. Using a placebo helps make study results fair and unbiased, because researchers and patients cannot tell who is taking a placebo, and who is taking the real medicine. In this study a placebo was given to patients once daily for 2 weeks at the beginning of the study. After this 2 week “run-in period” the patients were given 1 of the following treatments:

- Placebo once daily for up to 12 weeks
- 50 mg of mirabegron once daily for up to 12 weeks
- 100 mg of mirabegron once daily for up to 12 weeks

- 4 mg of tolterodine once daily for up to 12 weeks

Patients were picked for each treatment by chance alone.

Both men and women took part in the study. They were all over 18 years old. They had bladder problems for at least 3 months before the study. Patients could not take part in this study if they had the following conditions:

- Leakage of urine under stress conditions (exercise, laughing).
- Catheters (tube for draining urine) inserted in their bladders.
- Stones in their bladder.
- Received nondrug treatment, including electro-stimulation therapy, for their bladder problems.
- Radiation therapy in the lower abdomen or cancer in the lower abdomen.
- Infections of the structures that carry urine.
- Severe high blood pressure (greater than or equal to 180 mmHg systolic and/or greater than or equal to 110 mmHg diastolic while sitting down).
- Kidney disease caused by diabetes.

During this study, patients made 5 visits to the clinic and were contacted once by telephone. At first they were given a placebo to take for 2 weeks. Patients also kept a diary of their symptoms. At the end of the 2 weeks, patients returned to the clinic. During this visit, patients were selected to stay in the study if their diaries showed that during the previous 3 days:

- They were not able to control when to empty the bladder for at least 3 times
- And they had urinated at least 8 times a day.

A total of 2437 patients volunteered for the study and 2336 patients received placebo during the run-in period. A total of 1978 patients received placebo, mirabegron, or tolterodine for up to 12 weeks in this study and took the following once per day:

- 494 patients took placebo
- 493 patients took mirabegron 50 mg
- 496 patients took mirabegron 100 mg
- 495 patients took tolterodine 4 mg

	Number (out of 1978 patients)
Age Group	
Aged between 18 and 64 years	1244
Aged 65 years and older	734
Sex	
Men	549
Women	1429
Country where Clinic was Located	
EU	1689
Outside EU	289

What Were the Study Results?

The results of the study suggest that both mirabegron 50 and 100 mg pills treat the symptoms of overactive bladder better than placebo.

At the end of the study mirabegron was better than placebo in the following ways:

- Fewer leaking or wetting accidents per day
- Fewer episodes of urinating per day
- More urine passed each time a patient urinated

Mirabegron was better than placebo in treating the symptoms of bladder problems starting from week 4 until the end of the study.

At week 4, tolterodine was better than placebo in reducing the number of leaking or wetting accidents per day and the number of episodes of urinating per day. At the end of the study, tolterodine was better than placebo in increasing the urine produced each time a patient urinated.

What Adverse Reactions did Patient Have?

A lot of research is needed to know whether a drug 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 number of patients who experienced adverse reactions was similar for all 4 treatment groups. The table below shows the most common adverse reactions experienced by patients who received at least 1 dose of study medicine.

Adverse Reaction	Number of Placebo Patients (out of 494 patients)	Number of Mirabegron Patients		Number of Tolterodine Patients (out of 495 patients)
		50 mg (out of 493 patients)	100 mg (out of 496 patients)	
Increased blood pressure	23	20	23	30
Dry mouth	9	9	12	47
Headache	6	13	5	11

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. Four people in the placebo group, 3 in the mirabegron 50 mg group, 2 in the mirabegron 100 mg group and 6 in the tolterodine group had serious adverse reactions. There was 1 death in the tolterodine group, for which the study doctor could not exclude the possibility that it was related to tolterodine.

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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