Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-Blind, Parallel Group, Active Controlled, Multicenter Long-term Study to Assess the Safety and Efficacy of the Beta-3 Agonist Mirabegron (YM178) 50 mg qd and 100 mg qd in Subjects With Symptoms of Overactive Bladder. This is also known as the TAURUS 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 well tolerated and safe for patients over the long term. Also, it was important to find out what unwanted effects mirabegron might cause.

This study for mirabegron (also known by its brand names Betmiga ®, Myrbetriq ®, and Betanis ®) took place at 306 clinics in Europe, the United States, Canada, South Africa, Australia and New Zealand. The study took place from April 2008 to May 2010. 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 medicines (mirabegron or tolterodine).

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. 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:

- 50 mg of mirabegron once daily for up to 12 months
- 100 mg of mirabegron once daily for up to 12 months
- 4 mg of tolterodine once daily for up to 12 months

Patients were picked for each treatment by chance alone.

Some patients who completed a different mirabegron study were allowed to enroll in this study.

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 7 visits to the clinic. 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 2849 patients volunteered for the study and 2792 patients received placebo during the run-in period. A total of 2444 patients received mirabegron or tolterodine for up to 12 months in this study and took the following once per day:

- 812 patients took mirabegron 50 mg
- 820 patients took mirabegron 100 mg
- 812 patients took tolterodine 4 mg

	Number (out of 2444 patients)
Age Group	
Aged between 18 and 64 years	1536
Aged 65 years and older	908
Men	634
Women	1810
EU Countries	1339
Outside EU	1105

What Were the Study Results?

The results of the study suggest that the 2 doses of mirabegron (50 mg and 100 mg) were safe and well tolerated over the long term.

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 number of patients who experienced adverse reactions was similar for all 3 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 Mirabegron Patients		Total Number of Mirabegron Patients (out of 1632 patients)	Number of Tolterodine Patients (out of 812 pateints)
	50 mg (out of 812 patients)	100 mg (out of 820 patients)		
High blood pressure	43	50	93	42
Dry mouth	20	18	38	67
Constipation	18	17	35	19
Headache	18	14	32	14

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. Some patients had serious adverse reactions: 42 patients in the mirabegron 50 mg group, 51 patients in the 100 mg group, and 44 patients in the tolterodine group. No patients died during this 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 Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands