Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-blind, Parallel Group, Proof of Concept Study of YM178 in Comparison with Placebo and Tolterodine in Patients with Symptomatic Overactive Bladder. This is also known as the BLOSSOM study.

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 often than usual (called increased urinary frequency).
- Not being able to control the emptying of the bladder and lose urine involuntarily (called urge incontinence).

There are several medicines for overactive bladder in adults. They include mirabegron (also known as YM178 and Betmiga®, Myrbetriq® and Betanis®) and tolterodine (also known as Detrusitol and Detrol®).

This study was conducted in patients with overactive bladder. The study compared the effects of mirabegron and tolterodine to placebo tablets. Placebo tablets have no study medicine in them. This study helped answer which of these treatments was better at treating overactive bladder in these patients. This study looked at how often patients had to urinate per day. It was also important to find out what unwanted effects these patients had from the study treatments.

This study for mirabegron took place at 35 clinics in Belgium, Czech Republic, Germany, Spain, Sweden and the UK. The study took place from April 2004 to January 2005. 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 test medicine.

Both men and women could take part in the study if:

- They were 18 years or older.
- They were able to fill out a diary about their bladder problem symptoms.
- They had to empty their bladder often for at least 3 months before the study start. They also had a sudden need to urinate that was difficult to delay.

Patients could not take part in this study if:

- They were female patients who were pregnant, planning to become pregnant or were breastfeeding their baby. Or they were female patients who were using unreliable birth control methods.
- They had a blockage of the bladder preventing urine flowing out of the bladder properly.
- The amount of urine left in their bladder after urination was more than 200 mL.
- Most of the time, they had leakage of urine under stress conditions (exercise, laughing).
- The cause of their bladder problems was problems with the wiring of nerves to their bladder.
- They had nerve damage that was caused by diabetes and chronic high blood sugar.

During this study, the study doctor did a check-up of the patients at 6 study visits. At visit 1, patients were checked to see if they could be in the study. The patients then started a 2-week "run-in period." During this period, patients took placebo twice daily for 2 weeks. Patients also kept a diary of their bladder symptoms during the 3 days before the next visit. At visit 2, the diaries were checked to see if patients could remain in the study. Patients could remain in the study if their diaries showed that during the previous 3 days:

- They had urinated at least 8 times a day on average.
- They had a sudden need to urinate that was difficult to delay on at least 3 occasions.

Patients could not remain in the study if:

- They did not complete the diary as instructed.
- The daily maximum amount of their urine was on average more than 3 L.
- Blood levels of certain liver chemicals were higher than normal and higher than at visit 1.

Patients who could remain in the study were picked for 1 of the following treatments by chance alone:

- Placebo
- Mirabegron 100 mg twice daily
- Mirabegron 150 mg twice daily
- Tolterodine 4 mg once daily

Patients took study treatment for up to 4 weeks. The patients returned to the clinic for a check-up at weeks 1, 2 and 4 of study treatment (visits 3 through 5). After visit 5, patients took placebo for 2 weeks. Next, they returned to the clinic for the final check-up (visit 6).

A total of 314 patients were in this study. After the "run-in period," 262 patients could remain in the study and were picked for 1 of the study treatments by chance alone. A total of 260 patients took at least 1 dose of study treatment.

- 66 patients took placebo.
- 65 patients took mirabegron 100 mg twice daily.
- 65 patients took mirabegron 150 mg twice daily.
- 64 patients took tolterodine 4 mg once daily.

	Number of Patients (out of 260 patients)
Age Group	
Aged between 24 and 83 years	260
Sex	
Women	222
Men	38
Clinic Location	
EU Countries	260
Belgium	23
Czech Republic	104
Germany	76
Spain	14
Sweden	26
The UK	17
Outside EU	0

What Were the Study Results?

This study was conducted in patients with overactive bladder. The study compared the effects of mirabegron and tolterodine to placebo tablets. The study looked at how often patients had to urinate per day. On average, patients had to urinate 1 time fewer per day when they took mirabegron than when they took placebo. It did not matter which mirabegron dose patients took.

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 reactions experienced by patients who took at least 1 dose of study treatment. Headache or head pain was the most common adverse reaction. The number of patients who had headache or head pain was similar in all groups. More patients in the mirabegron (150 mg twice daily) and tolterodine groups than in the other groups had dry mouth. More patients in the mirabegron (150 mg twice daily) group than in the other groups reported dizziness (or sensation of lightheadedness, unsteadiness, or giddiness). More patients in the mirabegron (150 mg twice daily) group than in the other groups experienced vomiting. More patients in the mirabegron (150 mg twice daily) group than in the other groups experienced unpleasant sensation of irregular and/or forceful beating of the heart.

Adverse Reaction	Placebo (out of 66 Patients)	Mirabegron 100 mg Twice Daily (out of 65 Patients)	Mirabegron 150 mg Twice Daily (out of 65 Patients)	Tolterodine 4 mg Once Daily (out of 64 Patients)
Unpleasant sensation of irregular and/or forceful beating of the heart	1 (1.5%)	0	3 (4.6%)	0
Feeling of spinning or whirling	2 (3.0%)	0	1 (1.5%)	0
Diarrhea	0	1 (1.5%)	0	2 (3.1%)
Dry mouth	1 (1.5%)	0	4 (6.2%)	3 (4.7%)
Nausea or the urge to vomit	0	1 (1.5%)	1 (1.5%)	2 (3.1%)
Vomiting	0	1 (1.5%)	3 (4.6%)	0
Fatigue or tiredness	2 (3.0%)	0	0	0
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	0	1 (1.5%)	3 (4.6%)	1 (1.6%)
Headache or head pain	2 (3.0%)	3 (4.6%)	3 (4.6%)	4 (6.3%)
Widely spread skin rash	0	2 (3.1%)	0	0

An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or needs hospital care. Two patients had serious adverse reactions after they took tolterodine or placebo. One patient had a skin rash. The other patient had chest pain or discomfort that occurs when the heart does not get enough oxygen-rich blood.

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.

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