Summary of Results for Laypersons

Astellas is grateful to the patients who took part in this clinical study. Thank you.

What was the Study Called?

A Randomized, Double-blind, Parallel Group, Placebo and Active Controlled, Multi-Center Dose Ranging Study with the Beta-3 Agonist YM178 in Patients with Symptomatic Overactive Bladder. This study is also known as the DRAGON study.

Why was this Study Needed?

Mirabegron (also known as YM178) is a prescription medicine for overactive bladder (OAB) symptoms. In order to improve safety, a new form of the medicine was developed that allowed it to be gradually released in the body. This is called oral (taken by mouth) controlled absorption system (OCAS). Information was needed on how well this new form of the medicine worked at low, 2 medium and high doses in patients with OAB.

This study was conducted in patients with OAB. Patients took mirabegron (OCAS) at 1 of 4 dose levels. Or they took another prescription medicine for OAB called tolterodine SR. Or they took placebo. The section below describes what placebo tablets are. This study looked at the average number of times per 24 hours patients had to urinate. The study compared the changes after patients took low, 2 medium and high doses of mirabegron (OCAS) for 3 months. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in April 2006 and ended in March 2007. When the study ended, the sponsor of this study (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 "double-blinded" study. That means that the patients and the study doctors did not know who took which of the study medicines (mirabegron, tolterodine SR, 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 study doctors and patients cannot tell who is taking a placebo, and who is taking the test medicine. All patients in this study took the same number of tablets and capsules each day.

This study included women and men 18 years or older with OAB. Their symptoms included having to empty the bladder more often than usual. And they could not control the emptying of the bladder and lost urine involuntarily. They had these symptoms for at least 3 months or longer.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study took placebo for 2 weeks. During the last 3 days, patients kept a diary of their

OAB symptoms. Next, the study doctor checked the diaries to see if the patients could remain in the study. Patients who could remain in the study were picked for one of 6 treatments by chance alone. These were: 25, 50, 100 or 200 mg mirabegron OCAS, 4 mg tolterodine SR, or placebo. Patients took their assigned oral medicine (taken by mouth) once a day for 3 months.

This study took place at 97 clinics in 14 countries. 1108 patients were in the study. Out of these patients, 927 took at least 1 dose of their assigned study medicine.

	Mirabegron (673 patients)	**Tolterodine (85 patients)**	**Placebo (169 patients)**
Age Group			
Aged 65 years or younger	485	64	124
Aged older than 65 years	188	21	45
Sex			
Men	67	16	15
Women	606	69	154
Clinic Location			
European Union Countries (*at the time of the study*)			
Belgium	6	0	0
Czech Republic	147	21	42
Denmark	11	1	3
France	22	5	5
Germany	96	12	19
Hungary	29	5	17
Italy	46	2	15
Poland	91	10	20
Spain	24	4	4
Sweden	20	3	7
The Netherlands	42	3	11
United Kingdom	28	5	8
Outside European Union			
Norway	17	0	5
Russia Federation	94	14	13

What Were the Study Results?

This study was in patients with OAB. The study looked at the average number of times per 24 hours patients had to urinate. The study compared the changes after patients took low, 2 medium or high doses of mirabegron (OCAS) for 3 months.

After 3 months of treatment, patients had to urinate less frequently per 24 hours. Medium doses (50 mg, 100 mg) or high dose (200 mg) of mirabegron worked better at reducing number of urinations than the lowest dose (25 mg). Patients who took placebo had to urinate an average of 1.44 fewer times per 24 hours. It was an average of 1.88, 2.08, 2.12, and 2.24 fewer times per 24 hours for patients who took 25, 50, 100, or 200 mg mirabegron. A

statistical test showed that the differences from placebo were not likely to be due to chance in 50, 100, and 200 mg doses.

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 assigned study medicine in this study.

Adverse Reaction	mirabegron (out of 673 patients)	Tolterodine (out of 85 patients)	Placebo (out of 169 patients)
Any adverse reaction	145 (21.5%)	13 (15.3%)	26 (15.4%)
Headache or head pain	18 (2.7%)	1 (1.2%)	4 (2.4%)
Dry mouth	16 (2.4%)	3 (3.5%)	3 (1.8%)
Constipation	12 (1.8%)	1 (1.2%)	2 (1.2%)
Nausea or the urge to vomit	12 (1.8%)	1 (1.2%)	2 (1.2%)
Heartburn	6 (0.9%)	0	1 (0.6%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care.

Two patients (0.3% or 2 out of 673 patients) experienced serious adverse reactions in this study: 1 patient took 50 mg mirabegron, and 1 patient took 100 mg mirabegron.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of April 2010. You can find this summary and more information about this study 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. This summary only shows the results of this 1 study. Your doctor may help you understand more about the results of this study.

Sponsor contact details:

Astellas Pharma Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands