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 Phase 4, Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Mirabegron in Men with Overactive Bladder (OAB) Symptoms While Taking the Alpha Blocker Tamsulosin Hydrochloride for Lower Urinary Tract Symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH). This is also known as the PLUS study.

Why was this Study Needed?

Mirabegron is a prescription medicine for overactive bladder (or OAB for short). Symptoms that may be similar to OAB may also occur in men due to an enlarged prostate (also known as LUTS due to BPH). LUTS may occur due to both OAB and BPH at the same time. Tamsulosin is a prescription medicine for LUTS due to BPH but it fails to relieve OAB symptoms in some men. Therefore, there was a need to study mirabegron in men with OAB who are taking tamsulosin for their LUTS due to BPH.

This study was conducted in male patients with OAB who took tamsulosin for their LUTS due to BPH. The patients took mirabegron or placebo in this study. (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 study medicine (mirabegron or placebo) for 12 weeks. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in June 2016 and ended in September 2018. 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 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.

This study included men aged 40 years or older with OAB. Their symptoms included having to urinate at least 8 times per 24 hours. And they had a sudden need to urinate that was difficult to delay on at least 2 occasions per 24 hours. (This is known as urgency.) They had these symptoms for at least 3 months before the study started. They had been taking tamsulosin (0.4 mg once a day) for their LUTS due to BPH for at least 2 months.

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. Four weeks into the

study, they kept a diary of their OAB symptoms for 3 days. 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 a treatment (mirabegron or placebo) by chance alone.

- Mirabegron: Patients took mirabegron tablets (25 mg) once a day for 4 weeks. Thereafter, they took mirabegron tablets (50 mg) once a day for 8 weeks.
- Placebo: Patients took placebo tablets for mirabegron 25 mg once a day for 4 weeks. Thereafter, they took placebo tablets for mirabegron 50 mg once a day for 8 weeks.

In addition, patients continued to take their daily dose of tamsulosin (0.4 mg) throughout the study.

This study took place at 80 clinics in several countries. 1009 patients were in the study. After the diary check, 715 patients could remain in the study. Out of these patients, 706 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged 40 years to less than 65 years	307
Aged 65 years or older	399
Clinic Location	
European Union Countries (*at the time of the study*)	508
France	2
Germany	91
Italy	91
Poland	149
Czech Republic	103
Spain	49
The UK	23
Outside European Union	198
Canada	26
The US	172

What Were the Study Results?

This study in patients with OAB who took tamsulosin for their LUTS due to BPH looked at the average number of times per 24 hours patients had to urinate.

This study showed that after 12 weeks of treatment, patients had to urinate less frequently per 24 hours. Patients who took placebo had to urinate an average of 1.56 fewer times per 24 hours. It was an average of 1.95 fewer times per 24 hours for patients who took mirabegron. A statistical test showed that the difference was not likely to be due to chance.

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 medicine in this study.

Adverse Reaction	Mirabegron (out of 352 patients)	Placebo (out of 354 patients)
Any adverse reaction	42 (11.9%)	21 (5.9%)
Difficulty emptying the bladder	5 (1.4%)	0
Headache or head pain	5 (1.4%)	5 (1.4%)
Dry mouth	3 (0.9%)	0
High blood pressure	3 (0.9%)	5 (1.4%)
Frequent urge to urinate during the day	2 (0.6%)	1 (0.3%)
Upper belly pain	2 (0.6%)	1 (0.3%)

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

Three patients (0.4%, or 3 out of 706 patients) experienced serious adverse reactions in this study: 2 patients who took mirabegron and 1 patient who took placebo.

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 2019. 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.

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