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 3, Double-blind, Randomized, Placebo-controlled Study to Assess the Efficacy and Safety of ASP1941 in Combination with Metformin in Asian Patients with Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Metformin Alone

Why was this Study Needed?

Diabetes is a disease in which the blood sugar level is too high. Insulin is a hormone that helps transport the sugar from the blood into the cells. The sugar then becomes energy for the cells. In type 2 diabetes, the body does not use insulin properly. People with diabetes need to manage their disease to stay healthy. Diabetes can cause problems that may be disabling or even life-threatening. Metformin is an oral medicine (taken by mouth) for the treatment of type 2 diabetes. But in some patients, it may not work well enough. This means that metformin does not keep their blood sugar levels near the normal range. Therefore, there was a need to study a new treatment for type 2 diabetes. Ipragliflozin (also known as ASP1941 and Suglat®) is a new oral medicine for the treatment of type 2 diabetes. It works in a different way than metformin. Metformin works mostly by decreasing the amount of blood sugar produced by the liver. It also makes muscle tissue more sensitive to insulin, so that it absorbs blood sugar. Ipragliflozin works in the kidneys to reduce the reabsorption of sugar into the blood. This lowers blood sugar levels and increases the amount of sugar in the urine.

This study was conducted in Asian patients with type 2 diabetes. They were taking metformin but it did not work well enough. In this study, patients took ipragliflozin or placebo. (The section below describes what placebo tablets are.) The patients continued to take their prescribed dose of metformin. The main question this study helped answer was which of the study medicines (ipragliflozin or placebo) together with metformin lowered the patients' blood sugar levels more after 6 months. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in November 2011 and ended in January 2013. 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 study had 2 parts or periods: a "run-in period," followed by a "double-blinded period."

"Run-in period": The study doctors, but not the patients, knew that all patients took placebo during the 2-week run-in period.

"Double-blinded period": The patients and the study doctors did not know who took which of the study medicines (ipragliflozin or placebo) during the double-blinded period. 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 adult Asian women and men aged 20 years or older. They had type 2 diabetes for at least 3 months before the first study visit. They had been taking the same dose of metformin (1000 mg/day or more) for at least the past 2 months. The metformin did not work well enough. Their HbA1c level was between 7.0% and 10.0%. The HbA1c level is a measure of a patient's average level of blood sugar over the past 3 months. Their body mass index (BMI) was between 20 and 45. BMI is a measure of body fat in adults that is based on height and weight. An adult with a BMI of 25 or higher is overweight.

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. Starting at the second visit, all patients who could be in the study took placebo for 2 weeks. Thereafter, they were picked for a treatment (ipragliflozin or placebo) by chance alone. Patients were to continue to take their prescribed dose of metformin during the study.

- Ipragliflozin: Patients took 1 ipragliflozin tablet (50 mg) once a day for 6 months.
- Placebo: Patients took 1 placebo tablet once a day for 6 months.

This study took place at 30 clinics in Korea and Taiwan. 171 patients were in the study. Out of these patients, 170 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 65 years	141
Aged 65 years or older	29
Sex	
Men	77
Women	93
Clinic Location	
Outside European Union	170
Korea	82
Taiwan	88

What Were the Study Results?

This study was conducted in Asian patients with type 2 diabetes for whom metformin did not work well enough. This study looked at which of the study medicines (ipragliflozin or placebo) together with metformin lowered blood sugar levels more in these patients after 6 months.

Over the 6 months of treatment, the average HbA1c level decreased 0.94% in the ipragliflozin group. It decreased 0.47% in the placebo group.

A statistical test showed that the difference between the groups was not likely to be due to chance. The study showed that 6 months of ipragliflozin and metformin lowered sugar blood levels more than did placebo and metformin.

Visit	HbA1c Level	
	Ipragliflozin (out of 83 patients)	**Placebo (out of 85 patients)**
Start of treatment	7.74%	7.75%
End of treatment	6.82%	7.27%

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, study doctors 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	Ipragliflozin (out of 87 patients)	Placebo (out of 83 patients)
Any adverse reaction	17 (19.5%)	17 (20.5%)
Urinary tract infection	6 (6.9%)	2 (2.4%)
Decreased weight	3 (3.4%)	1 (1.2%)
Increased blood levels of liver enzymes	2 (2.3%)	0
Pain or discomfort when urinating	2 (2.3%)	3 (3.6%)
Itchy skin	1 (1.1%)	2 (2.4%)
Increased blood level of a liver pigment (bilirubin attached to sugars)	0	3 (3.6%)
Increased frequency of urination at night	0	3 (3.6%)
Increased urine level of the breakdown product of a hormone (norepinephrine)	0	2 (2.4%)

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

1 patient who took placebo experienced a serious adverse reaction.

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 August 2014. 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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