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, Randomized, Open-label, Active-controlled, Multicenter Study to Evaluate the Renal Protective Effect (UACR), Efficacy and Safety of Ipragliflozin in Type 2 Diabetes Mellitus Patients with Albuminuria.

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 produce as much insulin as is needed. Or the body does not use insulin properly. The resulting high blood sugar levels can damage the small blood vessels in the kidneys. When this happens, the kidneys can no longer filter the blood like they should. As a result, a protein (albumin) leaks from the blood into the urine. Albumin should be in the blood, not the urine. Oral (taken by mouth) medicines are available for treatment of type 2 diabetes. Metformin works mostly by decreasing the amount of blood sugar produced by the liver. Glimepiride works mostly by causing the pancreas to produce insulin. These medicines may not work well in all people with type 2 diabetes. Therefore, there was a need to study a new treatment for type 2 diabetes.

Ipragliflozin (also known as ASP1941) is an oral medicine for the treatment of type 2 diabetes. Ipragliflozin works in the kidneys to reduce the reabsorption of sugar into the blood. This lowers blood sugar levels. And it increases the amount of sugar in the urine.

This study was conducted in patients with type 2 diabetes. They did not have satisfactory control of their blood sugar. Patients took a combination of medicines in 1 of 2 treatment groups. They took metformin and ipragliflozin. Or they took glimepiride and metformin. The main question this study was meant to answer was which medicines made the leaking of blood albumin into urine less. This was measured by looking at the changes in UACR (Urine Albumin-to-Creatinine Ratio). UACR is a test that helps measure how severe this leakage from blood to urine is. A UACR of at least 30 means that the amount of albumin in the urine is more than normal. This is called albuminuria. It was also important to find out what unwanted effects the patients had from the study medicines.

The study started in April 2017. The sponsor (Astellas) stopped the study in December 2018. The reason was that not enough patients joined the study during the planned time. When the study was stopped, 33 patients had taken study medicine. 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 an “open-label” study. This means that each patient and the study doctors knew which combination of study medicines that patient took.

This study included Korean women and men aged 19 to 74 years. They had type 2 diabetes. They had been taking at least 1000 mg metformin each day for at least 8 weeks before the first study visit. They also had albumin leaking from their blood into their urine (UACR was at least 30). They had an HbA1c level between 7.0% and 9.0%. The HbA1c level is a measure of a patient's average level of blood sugar over the past 3 months. They had an estimated glomerular filtration rate (eGFR) that was at least 45. The eGFR is a blood test that looks at how well the kidneys are working.

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. If patients could be in the study, they were picked for 1 of 2 treatment groups by chance alone.

Patients took their prescribed dose of metformin that they had been taking before the study.

Treatment group 1: ipragliflozin and metformin: Patients took 1 tablet ipragliflozin (50 mg) each day. And they took metformin each day.

Treatment group 2: glimepiride and metformin: Patients took 1 tablet of glimepiride each day. The tablet could be 1 mg, 2 mg or 4 mg as per the study doctor's decision. And they took metformin each day.

Patients took their assigned medicines for 24 weeks.

This study took place at 17 clinics in Korea. 33 patients were in the study and took at least 1 dose of study medicine. 17 patients were in the glimepiride/metformin treatment group and 16 were in the ipragliflozin/metformin treatment group.

What Were the Study Results?

The main question this study was meant to answer was which medicines made the leaking of blood albumin into urine less. This was measured by the change in the UACR from start of the study to week 24.

When this study was stopped, there were not enough patients in the study to answer the study's main question. This is a summary of study results for the patients in the study.

From the start until the end of treatment, the median UACR decreased 16.4% in the glimepiride/metformin group. It increased 7.6% in the ipragliflozin/metformin group. Median is the middle number in a sorted list of numbers. The number of patients needed for doing meaningful statistical tests was not met.

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 adverse reactions experienced by patients who took at least 1 dose of study medicine in this study. There were no adverse reactions in the glimepiride/metformin group.

Adverse Reaction	**Ipragliflozin/Metformin (out of 16 patients)**
Any adverse reaction	2 (12.5%)
Headache or head pain	1 (6.3%)
Itching of the vulva and/or vagina (vulva=external female genitalia)	1 (6.3%)
Sudden severe potentially life-threatening damage to the lungs which can lead to fluid in the lungs	1 (6.3%)
Rash	1 (6.3%)

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

There were no serious adverse reactions in the study.

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 June 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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