Summary of Results for Laypersons

What was the Study Called?

A Phase 2, Double-Blind, Randomized, Placebo Controlled Study to Evaluate the Efficacy and Safety of ASP8232 as Add-On Therapy to Angiotensin Converting Enzyme inhibitor (ACEi) or Angiotensin Receptor Blocker (ARB) in Reducing Albuminuria in Patients with Type 2 Diabetes and Chronic Kidney Disease. This is also known as the ALBUM study.

Why was this Study Needed?

Insulin is a hormone that helps transport the sugar from the blood into the cells. The sugar then becomes energy for the cells. Type 2 diabetes is a disease in which the body makes little to no insulin or does not use insulin well. 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. One of the signs of diabetic kidney disease (or DKD for short) is when a protein (albumin) leaks from the blood into the urine. Albumin should be in the blood, not the urine. Albumin in the urine may increase the chances that the DKD progresses to kidney failure. DKD is treated with certain high blood pressure medicines. The decrease in blood pressure by these medicines can slow the progression of DKD. But the disease still progresses in some patients. Therefore, there was a need to study new treatments for DKD.

In this study, researchers looked at the effect of ASP8232 taken on top of the standard treatment for DKD. ASP8232 is an experimental medicine taken by mouth. It works by blocking a protein (vascular adhesion protein-1) in the body. Blocking that protein may prevent damage of the kidney blood vessels. This can be assessed by a decrease in the leakage of blood albumin into the urine. Such a decrease could slow the progression of DKD.

This study was conducted in patients who were taking standard treatment for their DKD. On top of their standard treatment, patients took either ASP8232 or placebo. (The section below describes what a placebo is.) The main question this study helped answer was which study medicine (ASP8232 or placebo) was better at decreasing the leakage of blood albumin into the urine. It was also important to find out what unwanted effects the patients had from the study medicines.

The study started in March 2015 and ended in March 2017. When this 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. That means that the patients and the researchers did not know who took which of the study medicines (ASP8232 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.

Clinical studies have a list of requirements for patients who can be in a study ("inclusion" criteria) and patients who cannot take part in a study ("exclusion" criteria). The requirements for this study are listed below.

Men and women aged between 18 and 85 years could take part in the study if:

- At study start, their estimated glomerular filtration rate (or eGFR for short) was at least 25 and was less than 75. eGFR is a blood test that looks at how well the kidneys are working.
- A doctor had confirmed that they had type 2 diabetes.
- Their average level of blood sugar over the past 3 months ("HbA1C level") was less than 11.0%.
- For the past 3 months, the dose of their standard treatment for their DKD had remained the same.
- A sample of their urine collected first thing in the morning contained between 200 and 3000 mg albumin per 1 g of creatinine (a substance normally eliminated by the kidneys into the urine). (A normal amount of albumin in urine is less than 30 mg per 1 g of creatinine.)

Patients could not take part in this study if:

- They had received a kidney transplant. Or they needed a treatment called "dialysis" to filter out wastes and extra salt and fluid from the blood. The kidneys normally do this filtering.
- Patient had a serious condition where urine cannot drain through the ureter (a tube that carries urine down from the kidneys to the bladder). Or the poor working condition of their kidneys was not related to a disease originating in the kidney. Or they had kidney disease that was the result of cancer.
- At study start or treatment assignment, they required treatment for a urinary tract infection or they had a serious infection.
- They had a health condition in addition to their DKD. The study doctor thought that that condition made it not possible for them to be in the study.

During the study, the study doctor did a check-up of the patients at periodic study visits. Several safety tests were also conducted to check patients' health. At visit 1, patients were checked to see if they could be in the study. Patients who could be in the study started a 5-week "pretreatment period." During this period, patients continued taking the same doses of their standard treatments for their type 2 diabetes and their DKD. On several days, urine samples were taken to measure the leakage of blood albumin into the urine. On the day of treatment assignment, patients were checked to see if they could remain in the study. Patients could remain in the study if their urine samples contained albumin.

Patients who could remain in the study were picked for 1 of 2 treatments by chance alone:

- ASP8232: Patients took 1 ASP8232 capsule (40 mg) by mouth once a day for 84 days.
- Placebo: Patients took 1 placebo capsule by mouth once a day for 84 days.

This study took place at 64 clinics in several countries. 125 patients were in the study and took at least 1 dose of study medicine.

	Number of Patients (out of 125 Patients)
Age Group	
Aged between 18 and 64 years	32
Aged between 65 and 84 years	93
Sex	
Men	96
Women	29
Clinic Location	
European Union countries (*at the time of the study*)	125
Czech Republic	20
Denmark	12
Germany	10
Hungary	23
Italy	9
Netherlands	7
Poland	19
Spain	19
United Kingdom	6
Outside European Union	0

What Were the Study Results?

This study in patients with DKD looked at the decrease of albumin leakage from the blood into the urine since the start of study treatment.

After 12 weeks of treatment, the leakage of blood albumin into the urine on average had decreased in the ASP8232 group, but not in the placebo group. Compared to treatment start, the albumin leakage after 12 weeks of treatment was approximately 18% (17.65%) lower in the ASP8232 group; and it was approximately 2% (2.31%) greater in the placebo group. Statistical testing showed that the difference in decrease of albumin leakage was not likely to be due to chance. It is considered to be an effect of the ASP8232 treatment.

The study showed that after 12 weeks of treatment, ASP8232 was better than placebo at decreasing the leakage of blood albumin into the urine.

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 adverse reactions experienced by 2 or more patients who took at least 1 dose of study medicine in this study.

Adverse Reaction	ASP8232 (out of 64 patients)	Placebo (out of 61 patients)
Any adverse reaction	16 (25.0%)	4 (6.6%)
Kidneys not working well	5 (7.8%)	0
Decreased score on the blood test that looks at how well the kidneys are working (estimated glomerular filtration rate)	3 (4.7%)	0
Diarrhea	2 (3.1%)	0
Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)	2 (3.1%)	0
Swelling in the arms and/or legs	2 (3.1%)	0
Awaken 2 or more times in the night to urinate	1 (1.6%)	1 (1.6%)
Itchy skin	1 (1.6%)	1 (1.6%)

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

None of the patients experienced serious adverse reactions.

One patient died during the study. This patient took ASP8232. The patient did not die because of the study medicine.

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 October 2017. 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.

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