Summary of Results for Laypersons

What was the Study Called?

A Phase 1 Study to Evaluate the Effect of Renal Impairment on the Pharmacokinetics, Pharmacodynamics and Safety of ASP8232 (Part 1) and a Multiple Dose, Placebo-controlled Exploratory Safety, Pharmacokinetic and Pharmacodynamic Study in Type 2 Diabetes Mellitus Subjects with Chronic Kidney Disease (Part 2)

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.

ASP8232 is an experimental medicine taken by mouth (oral). It works by blocking the activity of 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 was a phase 1 study. Phase 1 studies often involve healthy volunteers (healthy people). These studies may also involve people with certain health conditions. Phase 1 studies look at what the body does to the study medicine and what the study medicine does to the body.

This study consisted of 2 parts: part 1 and part 2.

During part 1, healthy people and people whose kidneys were not working well took a single oral dose of ASP8232. The main question part 1 helped answer was how ASP8232 was taken up, broken down, distributed through the body and removed from the body. Healthy people were compared with people whose kidneys were not working well. It was also important to find out what unwanted effects the people had from ASP8232.

During part 2, patients with type 2 diabetes and DKD took daily oral doses of ASP8232 or placebo for 28 days. (The section below describes what a placebo is.) The main question part 2 helped answer was how safe it was to take daily oral doses of ASP8232 for several days in a row; and how well patients with DKD tolerated that. It was also important to find out what unwanted effects the patients with DKD had from the study medicines.

The study started in September 2013 and ended in September 2014. 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?

Part 1 of this study was an "open-label" study. This means that the people in part 1 knew that they took ASP8232.

Part 2 of this study was a "blinded" study. This means that the patients in part 2 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 of who can be in a study ("inclusion" criteria) and who cannot take part in a study ("exclusion" criteria). The requirements for parts 1 and 2 of this study are listed below.

Part 1:

People aged between 35 and 80 years could be in part 1 of the study if:

- At study start, their body mass index (BMI) ranged from 18.5 to 34.0 and they weighed at least 50 kg. 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.
- At study start and on their first day at the clinic, the healthy people had an estimated glomerular filtration rate (or eGFR for short) of at least 80. eGFR is a blood test that looks at how well the kidneys are working.
- At study start and on their first day at the clinic, the people whose kidneys were not working well had an eGFR between 15 and 79.

People could not be in part 1 of the study if:

- They had a history of allergic conditions (including allergies to medicines, asthma, eczema or extreme allergic reactions, but excluding seasonal allergies).
- They had Gilbert's syndrome. This is a harmless condition in which the liver does not properly process bilirubin (a substance made by the breakdown of red blood cells).
- Within 1 week before their first day at the clinic, they had an illness that caused a fever; or they had symptoms of a viral, bacterial (including an infection of the upper respiratory tract [nose, sinuses, throat, wind pipe and voice box]) or fungal infection.

Part 2:

Patients aged between 35 and 80 years could be in part 2 of the study if:

- At study start, a doctor had confirmed that they had type 2 diabetes and DKD for at least 1 year.
- Their eGFR score was between 15 and 60.

- For at least 3 months before study start, the dose of their standard treatment for their DKD had remained the same. And their blood pressure had remained stable during that time.
- The dose of their standard treatment for their type 2 diabetes had remained the same. And their average level of blood sugar over the past 3 months ("HbA1C level") was less than 7.5%.

Patients with DKD could not be in part 2 of the study if:

- They had been in part 1 of the study.
- Within 3 months before study start, they had a serious health condition. The study doctor thought that this condition made it not possible for them to be in the study. This health condition did not have anything to do with their kidney disease or their well-controlled diabetes or high blood pressure.
- 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.
- At study start and on their first day at the clinic, they had abnormal electrical conduction within the heart.

What Happened during the Study?

Part 1:

The study doctor did a check-up of the people in part 1 at periodic study visits. At visit 1, the people were checked to see if they could be in part 1 of the study. At visit 2, the people who could be in part 1 were checked into the clinic. The next day, they received a single oral dose of ASP8232. They stayed in the clinic for a total of 9 days. During the clinic stay and at later study visits, blood samples were collected. The samples were used to check the amount of ASP8232 in the blood and check the people's health. To monitor the people's health, several safety tests were done: tests of blood and urine, tests of the electrical activity of the heart and vital sign measurements. The vital sign measurements included measurements of blood pressure, pulse and body temperature.

Part 2:

The study doctor did a check-up of the patients in part 2 at periodic study visits. At visit 1, the patients were checked to see if they could be in part 2 of the study. At visit 2, the patients who could be in part 2 were checked into the clinic. One or 2 days later, patients were picked for a treatment (ASP8232 or placebo) by chance alone. Twice as many patients were picked for ASP8232 as for placebo.

- ASP8232: Patients took a daily oral dose of ASP8232 for 28 days.
- Placebo: Patients took a daily oral dose of placebo for 28 days.

Patients stayed in the clinic for a total of 10 days. During the clinic stay and at later study visits, blood samples were collected. The samples were used to check the amount of

ASP8232 in the blood and check the patients' health. Several safety tests (like the ones in part 1 of the study) were done to monitor the patients' health.

This study took place at 3 clinics in 3 countries. 40 people were in part 1 of the study and took at least 1 dose of study medicine. 15 patients with DKD were in part 2 of the study and took at least 1 dose of study medicine.

	Part 1 Number of People (out of 40 People)	**Part 2 Number of Patients (out of 15 Patients)**
Age Group		
Aged 65 years or younger	32	10
Aged older than 65 years	8	5
Sex		
Men	24	11
Women	16	4
Clinic Location		
European Union countries (*at the time of the study*)	33	15
Bulgaria	20	10
Romania	13	5
Outside European Union	7	0
Moldova	7	0

What Were the Study Results?

Part 1:

Part 1 of this study looked at the overall amount of ASP8232 in the bloodstream after a single dose of ASP8232. This was found to be greater in people whose kidneys were not working well than in healthy people.

Part 1 of this study also looked at the highest concentration of ASP8232 in the blood that was measured after a single dose of ASP8232. This was found to be greater in people whose kidneys were not working well than in healthy people.

Part 2:

Part 2 of this study looked at how safe it was to take daily oral doses of ASP8232 for several days in a row; and how well patients with DKD tolerated that.

The safety tests done during part 2 showed no safety issues in patients with DKD who took a daily oral dose of ASP8232 for 28 days.

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.

None of the people in part 1 and none of the patients with DKD in part 2 experienced adverse reactions.

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 2016. 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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