Summary of Results for Laypersons

What was the Study Called?

A Phase 2a Enriched Enrollment Randomized Withdrawal Study to Assess Analgesic Efficacy and Safety of ASP8477 in Subjects with Peripheral Neuropathic Pain. This is also known as the MOBILE study.

Why was this Study Needed?

The peripheral nerves are the nerves outside of the spinal cord and brain. Peripheral neuropathic pain is caused by damage to these nerves (called "peripheral nerve damage"). This pain usually occurs in the hands and feet but can also occur in other body locations. The causes of different types of peripheral nerve damage are as follows.

- The chickenpox (herpes zoster) virus can cause a painful rash with blisters that break open and crust over ("shingles"). Shingles can result in pain even after the rash is gone ("postherpetic neuralgia").
- The cause of painful diabetic peripheral neuropathy, or diabetic nerve pain, is chronic high blood sugar and diabetes.
- The cause of human immunodeficiency virus-associated neuropathy is an infection with that virus.
- The cause of post-traumatic nerve injury is a surgery or trauma.
- The cause of other types of peripheral neuropathy is unknown.

There are already medicines for the treatment of peripheral neuropathic pain. Those medicines may cause unwanted effects or may not work in all patients.

ASP8477 is an oral "fatty acid amide hydrolase inhibitor." It may work by stopping the breakdown of natural pain relievers produced by the human body. These natural pain relievers work similar to the way substances in cannabis (marijuana) work. They relieve pain and inflammation (swelling and redness). They may work longer when their breakdown is stopped by ASP8477.

This study was conducted in patients with postherpetic neuralgia or diabetic nerve pain. They took ASP8477 tablets or placebo tablets daily by mouth. Placebo tablets have no study medicine in them. This study helped answer if ASP8477 reduced the average daily pain intensity more so than did placebo. It was also important to find out what unwanted effects these patients had from the study medicines.

This study for ASP8477 took place at 18 clinics in Poland, Czech Republic and the UK. The study took place from February 2014 to February 2015. When the 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?

Patients took study medicine during a total of 9 weeks. This was a "blinded" study. In this study, patients did not know who took ASP8477 or placebo. The researchers knew that all patients took placebo during the "run-in period" and took ASP8477 during the "single-blind period." During the last 3 weeks of treatment ("double-blind period"), the researchers did not know who took ASP8477 or placebo. A "placebo" is a dummy treatment such as a tablet or capsule that looks like the test 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.

Men and women could be in the study if:

- They were at least 18 years old.
- The study doctor determined that they had pain from diabetic nerve pain or postherpetic neuralgia.
- Their pain was at least 4 on a scale of zero ("no pain") to 10 ("pain as bad as you can imagine") at the study start. This pain was the average daily pain.

Patients with diabetic nerve pain could be in the study if:

- They had diabetes and their blood sugar level was acceptable per protocol at the study start. Diabetes is a disease in which the blood sugar level is too high.
- The level of their blood sugar was acceptable per protocol within 3 months before the study start.
- They had pain from diabetic nerve pain for at least 1 year.
- The study doctor and the patients confirmed that the symptoms from diabetic nerve pain in hands and feet (including pain) were stable. This was the case for at least 3 months before the study start.

Patients with postherpetic neuralgia could be in the study if:

- They still had pain at least 6 months after the herpes zoster rash had gone.

Patients could not take part in the study if:

- They had at least moderate pain that was caused by a condition other than diabetic nerve pain or postherpetic neuralgia.
- They had cancer within the last 5 years.
- Within 1 year before study start, they had a condition in which their blood pressure dropped when they stood up quickly. This is called "orthostatic hypotension." This condition caused them to feel dizzy or lightheaded or to faint.
- At the study start, within 3 minutes from lying down to standing up, they felt dizzy or lightheaded or they fainted.
- At the study start, their blood pressure was not within the normal range.
- In the past, they had symptoms of fainting; they had symptoms that come before fainting, such as lightheadedness, dizziness, severe weakness or blurred vision; they had

serious heart abnormalities; or they had serious blood pressure or pulse rate abnormalities.

The study had 11 visits. At visit 1, patients were checked to see if they could be in the study. At visit 2, patients who could be in the study started a 1-week "run-in period." Patients took placebo twice daily for 1 week. Patients also kept a diary of their daily pain. At visit 3, the diaries were checked to see if patients could remain in the study. Patients could remain in the study if their diaries showed that:

- They had recorded their daily pain on at least 5 days, including the 3 last days.
- Over the last 3 days, their pain ranged from 4 to less than 9 on a scale of zero ("no pain") to 10 ("pain as bad as you can imagine"). This pain was the average daily pain.

Patients who could remain in the study started the 4-week "single-blind period." The patients kept a diary of their daily pain. They took ASP8477 10 mg twice daily for 3 days. At visit 4, patients were checked for unwanted effects that they could not tolerate. If they had no such effects, they could remain in the study. Next, the patients took ASP8477 20 mg twice daily for 3 days. At visit 5, patients were checked for unwanted effects that they could not tolerate. If they had no such effects, they could remain in the study. The patients then took ASP8477 30 mg twice daily for 21 days. Visits 6 and 7 were after the patients had taken this dose for 3 and 7 days, respectively. At visits 6 and 7, patients were checked for unwanted effects that they could not tolerate. If they had no such effects, they could remain in the study. If the patients had unwanted effects that they could not tolerate, their ASP8477 dose was reduced to 20 mg twice daily. If ASP8477 20 mg twice daily did not result in unwanted effects that the patients could not tolerate, they could remain in the study. Visit 8 was at the end of the "single-blind period." At visit 8, the diaries were checked to see if patients could remain in the study. Patients could remain in the study if:

- They had completed the "single-blind period."
- The study medicine had reduced their pain by at least 30%.
- Their diaries showed that they had recorded their daily pain on 5 days per week on average.
- Their diaries showed that they had recorded their daily pain on 2 of the last 3 days of the "single-blind period."

Patients who could remain in the study were picked by chance alone to receive ASP8477 or placebo. Patients who were picked for ASP8477 took their most recent dose, which was 20 or 30 mg twice daily. Patients took ASP8477 or placebo for 3 weeks ("double-blind period"). Visits 9 and 10 were 1 and 3 weeks after visit 8, respectively. Visit 11 was 2 weeks after patients took their last dose of study medicine.

At all visits, patients returned to the clinic for a check-up. At some visits, blood samples were collected.

A total of 132 patients were in this study. After the "single-blind period," 71 patients could remain in the study and were picked for ASP8477 or placebo by chance alone. They took at least 1 dose study medicine.

- 37 patients took ASP8477.
- 34 patients took placebo.

	Number of Patients	
	Placebo (out of 34 Patients)	**ASP8477 (out of 37 Patients)**
Age Group		
Aged between 40 and 83 years	34	37
Sex		
Men	25	17
Women	9	20
Clinic Location		
EU Countries		
Czech Republic	18	21
Poland	16	16
The UK	0	0
Outside EU	0	0

What Were the Study Results?

This study was conducted in patients with postherpetic neuralgia or diabetic nerve pain. All patients took ASP8477 daily during the 4-week "single-blind period." Eligible patients whose pain was reduced by at least 30% were then picked by chance alone to receive ASP8477 or placebo. They took ASP8477 or placebo daily for 3 weeks ("double-blind period"). This study tested if the average daily pain intensity was lower with ASP8477 than with placebo. There turned out to be no difference between the ASP8477 and placebo treatments. The study showed that the average daily pain intensity was 0.13 lower with ASP8477. The study showed that it was 0.11 lower with placebo.

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 common adverse reactions experienced by patients who took at least 1 dose of study medicine during the "single-blind period." Each adverse reaction was experienced by 2 patients.

Adverse Reaction	Number of Patients ASP8477 (out of 116 Patients)
Swelling of the arms and/or legs	2 (1.7%)
Sensation of heaviness	2 (1.7%)
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	2 (1.7%)
Sleepiness, the state of feeling drowsy, ready to fall asleep	2 (1.7%)
Disorientation	2 (1.7%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. During the "single-blind period," none of the patients experienced a serious adverse reaction.

The table below shows the adverse reactions experienced by patients who took at least 1 dose of study medicine during the "double-blind period." Each adverse reaction was experienced by 1 patient.

Adverse Reaction	Number of Patients	
	Placebo (out of 34 Patients)	ASP8477 (out of 37 Patients)
Skin rash resulting from contact with a substance that causes an allergic reaction	0	1 (2.7%)
Increased appetite	0	1 (2.7%)
Muscle stiffness	0	1 (2.7%)
Diarrhea	1 (2.9%)	0
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	1 (2.9%)	0

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. During the "double-blind period," none of the patients experienced a serious adverse reaction.

Where Can I Learn More About This Study?

Astellas is not planning to conduct any more studies with ASP8477.

This summary of the clinical study results is available 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. If you have questions about ASP8477, please discuss these with your doctor.

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