Summary of Results for Laypersons

What was the Study Called?

A Randomized, Controlled, Long-term Safety Study Evaluating the Effect of Repeated Applications of QUTENZA™ plus Standard of Care versus Standard of Care alone in Patients with Painful Diabetic Peripheral Neuropathy. This is also known as the PACE 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 common 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.
- The cause of painful diabetic peripheral neuropathy, or diabetic nerve pain, is chronic high blood sugar and diabetes.
- The cause of human immunodeficiency virus (HIV)-associated neuropathy is an infection with that virus.
- The cause of post-traumatic nerve injury is surgery or trauma.

There are already medicines for the treatment of peripheral neuropathic pain. Those medicines may cause unwanted effects or may not work in all patients. The capsaicin 8% patch ("capsaicin patch") delivers capsaicin into the skin to the nerves that cause pain. The high doses of capsaicin in the patch overstimulate these nerves. The nerves then become less sensitive and can no longer produce pain signals.

This 1-year study was conducted in patients with diabetic nerve pain. All patients took their normal treatment for diabetic nerve pain. Some patients also had repeated applications of the capsaicin patch. At the start and end of the study, the patients completed a questionnaire. The questionnaire was about how their diabetic nerve pain interfered with their daily tasks. The study looked if the questionnaire score was lower at the end of the study than at the start. A score reduction meant that the diabetic nerve pain interfered less with the daily tasks. It was also important to find out what unwanted effects these patients had after the patch applications.

This study for the capsaicin patch (also known as Qutenza®) took place at 71 clinics in Belgium, Czech Republic, France, Germany, Italy, the Netherlands, Poland, Russia, Spain, Ukraine and the UK. The study took place from November 2011 to February 2014. 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?

All patients in this study knew that they received their normal treatment for diabetic nerve pain. Some patients received capsaicin patches with their normal treatment. The others did not receive capsaicin patches. The study doctors who did the clinical tests did not know which study treatment patients received.

Men and women could be in the study if:

- They were at least 18 years old.
- They had diabetic nerve pain for at least 1 year before the study start.
- Their diabetic nerve pain was confirmed by at least 3 abnormal items found when the study doctor examined their feet.
- The level of their blood sugar was acceptable per protocol within 3 to 6 months before the study start.
- They took medicines to manage their blood sugar for at least 6 months before the study start.
- Their pain was at least 4 on a scale of zero ("no pain") to 10 ("pain as bad as you can imagine") before the study start. This pain was the average pain over the last 24 hours.

Patients could not take part in the study if:

- Their worst diabetic nerve pain was in their ankles or above.
- There was not a clear difference between their pain and pain from conditions other than diabetic nerve pain.
- They had at least moderate pain that was caused by a condition other than diabetic nerve pain.
- They had, or used to have, a foot ulcer.
- They had an amputation of a leg or a foot.
- They had advanced chronic kidney disease or they had kidney failure.

The study had 9 visits scheduled over a 1-year period. At visit 1, patients were checked to see if they could be in the study. At visit 2, patients who could stay in the study were picked for 1 of the following study treatments by chance alone:

- Capsaicin patches (applied for 30 minutes) and their normal treatment for diabetic nerve pain;
- Capsaicin patches (applied for 60 minutes) and their normal treatment for diabetic nerve pain;
- Their normal treatment for diabetic nerve pain.

The capsaicin patches were put on up to 4 painful spots on the feet at visit 2. Patients returned to the clinic every 2 months for visits 3 through 8. Patient received new patch applications at those visits. If the pain came back sooner, patients could receive a new patch application at intervals of at least 8 weeks. Patients could receive up to 7 patch applications over the study period. Visit 9 was the last study visit. For patients who had a patch application at visit 8, visit 9 was 8 to 12 weeks thereafter. Visit 9 was between weeks 52 and 56 for patients who had no patch application at visit 8.

A total of 468 patients were in this study and received at least 1 dose of study treatment.

- 156 patients received capsaicin patches for 30 minutes. They also received their normal treatment for diabetic nerve pain.
- 157 patients received capsaicin patches for 60 minutes. They also received their normal treatment for diabetic nerve pain.
- 155 patients received their normal treatment for diabetic nerve pain. They received no capsaicin patches.

	Number of Patients (out of 468 patients)
Age Group	
Aged between 18 and 64 years	308
Aged 65 years and older	160
Sex	
Men	224
Women	244
Clinic Location	
EU Countries	265
Belgium	7
Czech Republic	100
France	11
Germany	39
Italy	5
The Netherlands	15
Poland	81
Spain	1
The UK	6
Outside EU	203
Russia	92
Ukraine	111

What Were the Study Results?

All 468 patients in this study received their normal treatment for diabetic nerve pain for 1 year. Patients in this study were picked for a study treatment by chance alone. Of the 468 patients, 313 patients had repeated applications of the capsaicin patch. At the start and end of the study, the patients completed a questionnaire. The questionnaire was about how their diabetic nerve pain interfered with their daily tasks. The study looked if the questionnaire score was lower at the end of the study than at the start. A lower score meant that the diabetic nerve pain interfered less with the daily tasks. This study showed that the score reduction was greater for patients who received capsaicin patches than for those who did not. After capsaicin patches were put on for 30 minutes, the score was about a quarter lower than it was at study start. (The precise score reduction was 27.6%.) After capsaicin patches were put on for 60 minutes, the score was a third lower than it was at study start. (The precise score reduction was 32.8%.) For patients who received no capsaicin patches,

the score was a tenth lower than it was at study start. (The precise score reduction was 6.7%.)

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 most common adverse reactions experienced by patients who received at least 1 capsaicin patch. They also received their normal treatment for diabetic nerve pain. More patients had leg and/or arm pain after the patch was applied for 60 minutes than after it was applied for 30 minutes. The number of patients with other adverse reactions was similar between the 2 groups.

Adverse Reaction	Capsaicin Patch Applied for 30 Minutes and Normal Treatment for Diabetic Nerve Pain (out of 156 patients)	Capsaicin Patch Applied for 60 Minutes and Normal Treatment for Diabetic Nerve Pain (out of 157 patients)
Pain where the study patch was applied	44 (28.2%)	46 (29.3%)
Superficial reddening of the skin where the study patch was applied	12 (7.7%)	14 (8.9%)
Burning sensation	14 (9.0%)	15 (9.6%)
Leg and/or arm pain	6 (3.8%)	13 (8.3%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. Two patients experienced a serious adverse reaction. The table below shows these serious adverse reactions.

Serious Adverse Reaction	Capsaicin Patch Applied for 30 Minutes and Normal Treatment for Diabetic Nerve Pain (out of 156 patients)	Capsaicin Patch Applied for 60 Minutes and Normal Treatment for Diabetic Nerve Pain (out of 157 patients)
Chest pain or discomfort that occurs when the heart does not get enough oxygen-rich blood	0	1 (0.6%)
Cancer of the rectum	0	1 (0.6%)
Rapid and sudden increase in blood pressure	0	1 (0.6%)

Four patients died during the study. The patients did not die because of capsaicin patches.

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand capsaicin patches.

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 capsaicin patches, please discuss these with your doctor.

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