Summary of Results for Laypersons

What was the Study Called?

A Phase III, Double-blind, Randomized, Placebo-controlled, Multicenter Study Evaluating the Efficacy and Safety of QUTENZA® in Subjects with Painful Diabetic Peripheral Neuropathy. This is also known as the STEP 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.

In this study, patients with diabetic nerve pain received a single treatment with study patches. The study patches had capsaicin or no test medicine ("placebo") in them. This study tested if the pain intensity after patch application was lower between study weeks 2 and 8 than at the study start. This study helped answer if the capsaicin patch reduced the pain intensity more than did the placebo patch. This study looked at the average daily pain. It was also important to find out what unwanted effects these patients had from the study patches.

This study for the capsaicin patch (also known as Qutenza®) took place at 29 clinics in the US. The study took place from February 2012 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?

This was a "blinded" study. In this study, the patients and the researchers did not know who took which study patch (capsaicin or placebo). The study doctors who did the clinical tests did not know the treatments of the patients either. The placebo patch is a dummy treatment that looks like the capsaicin patch, but does not have any medicine in it. Using a placebo

patch helps make study results fair and unbiased, because researchers and patients cannot tell who is taking a placebo patch, and who is taking the patch with the test medicine (capsaicin).

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 start of the study.
- 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.
- Between study visits 1 and 2, their pain was at least 4 on a scale of zero ("no pain") to 10 ("pain as bad as you can imagine"). This pain was the average pain over the last 24 hours.
- Between study visits 1 and 2, they recorded their pain at least 6 days in a row.

Patients could not take part in the study if:

- Their worst diabetic nerve pain 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 feelings of depression or anxiety that were more intense than was allowed in this study.

The study had 6 visits. At visit 1, patients were checked to see if they could be in the study. If patients could be in the study, they kept a daily record of their pain for 7 to 12 days. At visit 2, patients who could stay in the study were picked by chance alone for their single treatment with study patches. Their treatment was either a capsaicin patch or a placebo patch. The study patches were put on up to 4 painful spots on the feet. The study patches were removed after 30 minutes. Patients returned to the clinic every 2 weeks for a check-up (visits 3 and 4). After visit 4, they returned to the clinic every 4 weeks for a check-up (visits 5 and 6). Visit 6 was the last study visit.

A total of 369 patients were in this study and received a study patch.

- 186 patients received capsaicin patches.
- 183 patients received placebo patches.

	Number of Patients (out of 369 patients)
Age Group	
Aged between 18 and 64 years	210
Aged between 65 and 74 years	106
Aged 75 years and older	53
Sex	
Men	215
Women	154
Clinic Location	
EU Countries	0
Outside EU	369
The US	369

What Were the Study Results?

In this study, patients with diabetic nerve pain received a single treatment. Their treatment was either a capsaicin patch or a placebo patch. This study tested if the pain intensity after patch application was lower between study weeks 2 and 8 than at the study start. This study looked at the average daily pain. This study showed that treatment with the capsaicin patch reduced pain more than did treatment with the placebo patch. Treatment with the capsaicin patch reduced pain by 27.44% on average. Treatment with the placebo patch reduced pain by 20.85% on average.

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 study patch. More patients in the capsaicin patch group than in the placebo patch group had these adverse reactions.

Adverse Reaction	Capsaicin Patch (out of 186 patients)	Placebo Patch (out of 183 patients)
Burning sensation	26 (14.0%)	4 (2.2%)
Pain where the study patch was applied	18 (9.7%)	4 (2.2%)
Leg and/or arm pain	17 (9.1%)	8 (4.4%)

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

None of the patients died during the study.

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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