Summary of Results for Laypersons

What was the Study Called?

QUTENZA™ versus Pregabalin in Subjects with Peripheral Neuropathic Pain: an Open-label, Randomized, Multicenter, Non-inferiority Efficacy and Tolerability Study. This is also known as the ELEVATE 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. They include lidocaine cream to put on the skin and pregabalin capsules to take by mouth. 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.

The patients in this study had peripheral neuropathic pain. For their pain, the patients received a single capsaicin patch treatment or they took pregabalin capsules daily. The main question this study helped answer was if the capsaicin patch was not worse than pregabalin at treating the pain. The study looked at the proportion of patients whose pain was reduced by at least 30% 8 weeks after the start of study treatment (called "responders"). This pain was the average pain over the last 24 hours. It was also important to find out what unwanted effects these patients had from the study medicines.

This study for the capsaicin patch (also known as Qutenza®) took place at 92 clinics in Armenia, Austria, Belarus, Belgium, Bulgaria, Czech Republic, Finland, France, Germany, Greece, Hungary, Italy, Poland, Portugal, Romania, Russia, Slovakia, Slovenia, Spain, Sweden, Turkey and the UK. The study took place from July 2012 to September 2013. 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 an "open-label" study. All patients knew that they received capsaicin patches or that they took pregabalin.

Men and women took part in the study. They could be in the study if:

- They were between 18 and 80 years old and in good health according to the study doctor.
- They had peripheral neuropathic pain. Their diagnosis was probable or definite.
- Their peripheral neuropathic pain was in a specific spot. This spot was easy to treat with the capsaicin patch.
- At study start, they had 1 of the following types of peripheral nerve damage:
  - They had postherpetic neuralgia. They still had pain at least 6 months after the blisters crusted over.
  - They had post-traumatic nerve injury at least 3 months after a surgery or trauma.
  - They had peripheral nerve damage that caused pain in several spots and was not diabetic nerve pain. They had the pain for at least 3 months. The pain could be located with certain tests.
- 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. They had this pain on at least 4 days in a row before the study start.
- The skin of the painful spots was dry and was not damaged or irritated.

Patients could not take part in the study if:

- They had significant pain. This pain was not caused by postherpetic neuralgia or by post-traumatic nerve injury. This pain was also not caused by peripheral nerve damage with pain in several spots that is not diabetic nerve pain.
- They had chronic pain in an arm, leg, hand or foot, usually after that limb had been injured.
- They had neuropathic pain because they used to get radiation treatment. They had diabetic nerve pain. Or they had HIV-associated neuropathy.
- Their painful spots were only on their face, above their hairline and/or close to tissues that secrete mucus.
- They could no longer feel heat in the painful spot. This indicates that the nerves no longer work.
- Their daily pain was 10 on a scale of zero ("no pain") to 10 ("pain as bad as you can imagine"). This was the case on at least 4 days between study visits 1 and 2.

The study had 5 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 4 to 12 days. At visit 2, patients who could stay in the study were picked for treatment 1 or 2 by chance alone.

- Treatment 1 was a single treatment with capsaicin patches. Lidocaine 4% cream was put on the skin. One hour later, the cream was removed and the capsaicin patches were put on up to 4 painful spots. The capsaicin patches were removed from the feet after

30 minutes. The capsaicin patches were removed from other body locations after 60 minutes.

- Treatment 2 was a daily dose of pregabalin capsules. Patients picked for this treatment started with a daily dose of 75 mg. Their daily dose was increased to 150 mg after 3 to 4 days. To determine the best dose for each patient, the daily dose was increased by 75 mg every 3 or 4 days. The dose was considered best for the patient when it reduced the pain by at least 30% compared to the study start. This dose also did not cause unwanted effects that the patient could not tolerate. Starting at 4 weeks after visit 2, the daily dose remained constant. The final daily dose could range from 150 to 600 mg.

The patients returned to the clinic every 2 weeks for a check-up (visits 3 and 4). Four weeks after visit 4, they returned for the last check-up (visit 5). Visit 5 was the last study visit.

A total of 586 patients were in this study. A total of 559 patients took study treatment.

- A total of 282 patients received a single treatment with capsaicin patches.
- A total of 277 patients took a daily dose of pregabalin.

	Capsaicin Patch (out of 282 patients)	**Pregabalin (out of 277 patients)**
Age Group		
Aged between 18 and 64 years	203	206
Aged 65 years and older	79	71
Sex		
Men	123	122
Women	159	155
Clinic Location		
EU Countries	206	202
Austria	5	3
Belgium	11	11
Bulgaria	28	26
Czech Republic	3	3
Finland	3	1
France	17	17
Germany	14	15
Greece	10	10
Hungary	5	4
Italy	16	17
Poland	32	33
Portugal	2	1
Romania	31	31
Slovakia	6	8
Slovenia	2	0
Spain	4	5
Sweden	2	2
The UK	15	15
Outside EU	76	75
Armenia	19	21
Belarus	5	3
Russia	28	27
Turkey	24	24

What Were the Study Results?

The patients in this study had peripheral neuropathic pain. For their pain, the patients received a single capsaicin patch treatment or they took pregabalin capsules daily. The study looked at the proportion of patients who completed whose pain was reduced by at least 30% 8 weeks after the start of study treatment. This pain was the average pain over the last 24 hours. The proportion of capsaicin patch responders was 55.7%. The proportion of pregabalin responders was 54.5%. A test compared the capsaicin patch and pregabalin responders. The value of 0.693 was selected as a meaningful difference between the 2 treatments. The test result was 1.034 and its accuracy ranged from 0.715 to 1.496. Thus, the lower value for accuracy was greater than 0.693. This meant that the single capsaicin patch treatment was no worse than the daily dose of pregabalin at treating pain.

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 took study treatment. Patients in the capsaicin patch group had adverse reactions that were at the spots where the patches were put on the skin. Those adverse reactions were pain, superficial reddening of the skin where the patch was applied and burning sensation. None of the patients in the pregabalin group had those adverse reactions. More patients in the capsaicin patch group than in the pregabalin group had superficial reddening of the skin. The location of the skin reddening was not specified. More patients in the capsaicin patch group than in the pregabalin group had pain. There were several adverse reactions in the pregabalin group that did not happen in the capsaicin patch group. These were dizziness (or sensation of lightheadedness, unsteadiness, or giddiness); sleepiness, the state of feeling drowsy, ready to fall asleep; weight gain; and feeling of spinning or whirling. More patients in the pregabalin group than in the capsaicin patch group had nausea and headache.

Adverse Reaction	Capsaicin Patch (out of 282 patients)	Pregabalin (out of 277 patients)
Pain where the study patch was applied	67 (23.8%)	0
Superficial reddening of the skin (location not specified)	59 (20.9%)	1 (0.4%)
Burning sensation	44 (15.6%)	0
Superficial reddening of the skin where the study patch was applied	25 (8.9%)	0
Pain	15 (5.3%)	2 (0.7%)
Headache or head pain	3 (1.1%)	26 (9.4%)
Nausea or urge to vomit	1 (0.4%)	30 (10.8%)
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	0	51 (18.4%)
Feeling of spinning or whirling	0	14 (5.1%)
Sleepiness, the state of feeling drowsy, ready to fall asleep	0	43 (15.5%)
Weight gain	0	17 (6.1%)

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

Serious Adverse Reaction	Capsaicin Patch (out of 282 patients)	Pregabalin (out of 277 patients)
Inability of the heart to adequately pump blood to supply oxygen to the body	0	1 (0.4%)
Swollen tongue	0	1 (0.4%)
Second degree burn of the skin where the study patch was applied	1 (0.4%)	0
Study patch applied longer than allowed	1 (0.4%)	0

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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