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Long-term treatment with capsaicin 8% patches: a subgroup analysis in patients with post-herpetic neuralgia from an open-label study

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Introduction

Painful neuropathy or peripheral neuropathic pain (PNP) is estimated to be experienced by about 7–8% of the European population and can have a significant impact on quality of life. It is considered to be a distinct chronic pain condition according to the revised International Association for the Study of Pain (IASP) recommendations for ICD11 [1], and is challenging to manage. Post-herpetic neuralgia (PHN) following shingles infection, is one of the conditions of PNP.

Capsaicin is a highly selective, potent agonist of transient receptor potential cation channel subfamily V member 1 (TRPV1) receptors. Through a combination of activities it defunctionalizes nociceptor fibers and reduces cutaneous hypersensitivity. As a result, capsaicin is an attractive treatment to control localized pain, hyperalgesia or allodynia [2]. The high concentration 8% capsaicin patch (HCCP) is commonly recommended as a second line therapy for PHN. It is indicated for the treatment of PNP in Europe and for the treatment of neuropathic pain associated with PHN and with diabetic peripheral neuropathy of the feet in the USA. HCCP delivers the drug effectively and directly to the skin, while limiting the risk of systemic effects and drug-drug interactions. Whilst controlled trials have demonstrated the safety and effectiveness of HCCP, the STRIDE study was designed to investigate the long-term safety of repeated patch administration in patients with non-diabetic neuropathic pain [3]. The present analysis considers the effect on treatment outcomes among a subgroup of patients with PHN included in the STRIDE study.

Methods

The STRIDE study was an open-label, multicenter, 52-week observational trial conducted in Europe. A diagnosis of PHN was based on pain persisting since shingles vesicle crusting, for a minimum of 3 months. Prior treatment with capsaicin patches and a history of diabetes were among the exclusion criteria. Patients received up to 6 HCCP (capsaicin 640 g/cm^2; 8% weight for weight) treatments at 9- to 12-week intervals. At each application visit, a maximum of 4 patches equivalent to an area of up to 1120 cm^2 were applied for 60 minutes. HCCP retreatment was at the investigator's discretion and according to patient feedback. Long-term tolerability and safety were the primary objectives of the study. In addition, areas of spontaneous pain and allodynia were monitored, and various scales were used to assess pain, quality of life and overall treatment outcome at each retreatment assessment time-period. Descriptive statistics (including means and standard deviations) are presented; missing observations were not imputed.

Results

Of the 107 PHN patients included in the study, 66 completed the trial. The reason for withdrawal was lack of efficacy in 16 (15%), adverse events in 5 (4.7%) and other reasons in 20 (18.7%). HCCP was applied only once in 22 patients, twice in 26, three times in 24 and ≥ 4 times in 35. All but 1 patient used preapplication topical anesthesia during the study, and 79.4% used concomitant medications for neuropathic pain (Table 1).

73% of patients reported possible or probable drug-related adverse events, mostly transient application site reactions (57.9%). The maximum severity was mild or moderate in 57% of cases, and only 1 drug-related event required treatment discontinuation.

Table 1. Pain Medication Used by >5% of Patients During the Study

Medication Class	Patients with PHN (n=107)
Overall	**85 (79.4)**
Analgesics	**77 (72.0)**
Other analgesics and antipyretics	60 (56.1)
Anilides	32 (29.9)
Other opioids	19 (17.8)
Natural opium alkaloids	23 (21.5)
Analgesics	9 (8.4)
Antiepileptics	**68 (63.6)**
Other antiepileptics	60 (56.1)
Benzodiazepine derivatives	9 (8.4)
Psychoanaleptic drugs	**28 (26.2)**
Nonselective monoamine reuptake inhibitors	15 (15.0)
Other antidepressants	12 (11.2)
Urological agents	**14 (13.1)**
Anti-inflammatory and antirheumatic products	**7 (6.5)**
Topical products for joint and muscular pain	**7 (6.5)**
Cardiac therapy	**12 (11.2)**
Anti-inflammatory products for vaginal administration	**5 (4.7)**

The change in average daily pain, from baseline to the end of treatment, is shown in Figure 1. The average daily pain score was reduced from a baseline value of 6.6 (SD, 1.46) to 5.0 (1.99) after 6 months and 4.6 (2.18) after 12 months. The overall change in mean daily pain intensity by the end of the study was approximately -1.7. The proportion of responders

Figure 1. Change from baseline in average daily pain in PHN patients receiving capsaicin patches at baseline and, on average, at months 4, 8 and 11

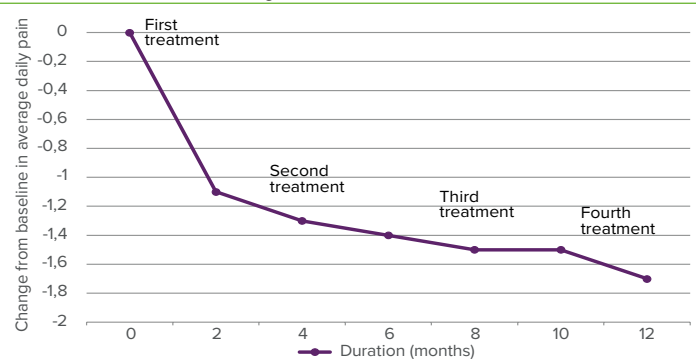
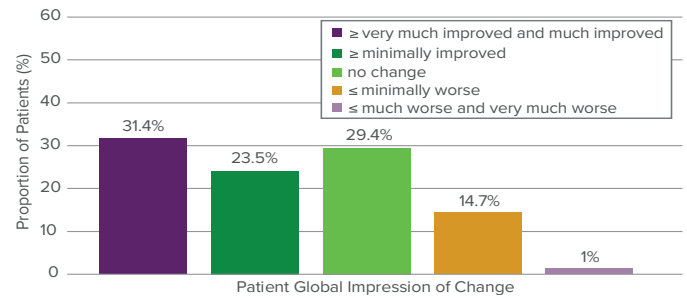


Figure 2. Patient Global Impression of Change (PGIC) by the end of the study (n=102 with non-missing data)



(≥ 30% decrease from baseline on a Numerical Pain Rating Scale) progressively increased during the study, to 22.7% after 3 months, and 33.3% and 39.7% after 6 and 12 months, respectively. Patient assessment of their condition by the end of study is presented in Figure 2; over 50% showed at least minimal improvement.

The area of allodynia/hyperalgesia and the extent of spontaneous pain (reported in most patients at baseline, mainly on the torso) decreased during the study by just over 20%, as shown in Table 2.

Table 2. Allodynia and spontaneous pain in PHN patients before and after treatment with capsaicin patches

Parameter	Baseline	End of Study
Area of allodynia/ hyperalgesia - mean (SD)	251.1 (219.5)	192.3 (212.8)
Area of spontaneous pain - mean (SD)	327.2 (235.2)	254.0 (225.6)

Conclusions

Repeated applications of HCCP over 12 months in patients with PHN are well tolerated and effective. Most adverse events were transient and local to the site of application. Progressive and sustained reduction in pain intensity was achieved, as well as reductions in the area of allodynia and spontaneous pain.

References

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Disclosures of Interest

Christopher G. Gharibo has been an advisor to Grünenthal GmbH.
Mariëlle Eerdekens and Sylvia Engelen are full-time employees of Grünenthal GmbH.
Lizandra Marcondes is a full-time employee of GRT US Holding Inc.
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