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Is repeat treatment with high concentration capsaicin patch beneficial in patients with peripheral neuropathic pain who did not respond after a first treatment?

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Introduction

High concentration capsaicin patch (HCCP; 179 mg or 8% w/w) is indicated for the treatment of peripheral neuropathic pain (PNP) in Europe and for the treatment of neuropathic pain associated with post-herpetic neuralgia (PHN) and with diabetic peripheral neuropathy (DPN) of the feet in the USA. HCCP can be administered in adults as monotherapy or in combination with other medications for chronic neuropathic pain. Pain relief is rapid and sustained after a single application, and treatment can be repeated approximately every 3 months.

In a 52-week randomized, controlled clinical trial (PACE study) in patients with painful DPN, which involved repeated HCCP applications, HCCP demonstrated greater efficacy than standard of care [1]. The magnitude of the differential treatment effect increased over time from the first to the last patch application. Likewise, in a 52-week trial in patients with non-diabetic PNP (STRIDE study), those who received four consecutive HCCP treatments (n=100) displayed a reduction in average daily pain scores [2].

The published literature does not provide details of responder rates beyond the first application of HCCP. In particular, the question remains open as to whether patients assessed as non-responders following a first application become responders after a second or subsequent applications. The present *post-hoc* analysis of data from the PACE and STRIDE studies investigates this question by considering a subset of subjects defined as initial non-responders.

Methods

In the two selected trials of 52-week duration, HCCP was applied for 30 min to the feet or 60 min to other body areas. All patients were diagnosed with PNP (painful DPN in PACE and non-diabetic PNP in STRIDE) and had an average daily pain score ≥4 on Question 5 of the Brief Pain Inventory or the Brief Pain Inventory-Diabetic Neuropathy scale. In the STRIDE study, repeat treatment was allowed every 9–12 weeks whereas, in the PACE study, repeat treatment was allowed after an interval of at least 8 weeks. Initial non-responders were defined as patients having a <30% decrease on the Numeric Pain Rating Scale (NPRS) from baseline to 3 months post-baseline. Responders were defined as patients who achieved a ≥30% decrease on the NPRS at predefined time-points (months 6, 9 and 12).

Results

Demographic details of the patients included in the STRIDE and PACE studies are presented in Table 1.

In the STRIDE study, 306 patients received an initial application of HCCP; at 3 months, data were available for 269 patients and, of these, 206 patients (76.6%) were assessed as non-responders. A total of 168 non-responders had a repeat treatment and 115 of these patients (68.5%) were still enrolled in the trial at 12 months. By comparison, from the total trial population (responders and non-responders), 174 patients (56.9%) were still enrolled in the trial after 12 months. Figure 1 shows the response rate at 3 months and the differential rates at 12 months (in patients still enrolled) between the 3-month non-responders and all patients. Of the initial non-responders who were still in the trial at 12 months (n=115), 57.4% of patients received at least four applications of HCCP and 33.9% had become responders to HCCP treatment. By comparison, 43.7% of all patients still enrolled at 12 months could be classified as responders.

Table 1. Demographic details of patients who received HCCP in the STRIDE study [2] and the PACE study [3] (safety analysis sets).

Characteristics	STRIDE	PACE
Number of patients	306	313
Diagnosis	non-diabetic PNP	PDPN
Gender (m/f)	174/132	153/160
Ethnicity (% Caucasian)	93	99
Mean age (years)	57.9	61
Mean time since pain diagnosis (years)	5.1	4.25
Mean baseline pain severity	6.2[a]	5.6[b]
Use of pain medications before baseline (% patients)	10	45

[a] Brief Pain Inventory questions 3-6. [b] Brief Pain Inventory diabetic neuropathy question 5.
Abbreviations: PNP – peripheral neuropathic pain; PDPN – painful diabetic peripheral neuropathy.

In the PACE study, after 3 months, 54.1% of patients who received an initial treatment with HCCP (n=313) did not meet the responder criteria. Of these 152 non-responders, 127 (83.5%) were still enrolled in the trial at 12 months. By comparison, from the total population (responders and non-responders), 250 patients (79.9%) were still enrolled in the trial after 12 months. Figure 2 shows the response rate at 3 months and the differential rates at 12 months (in patients still enrolled) between the 3-month non-responders and all patients.

Figure 1. Response rates (≥30 decrease in NPRS) to HCCP in PNP patients included in the STRIDE study [2] after 3 months, and at 12 months among non-responders at 3 months, and all patients still enrolled at 12 months.

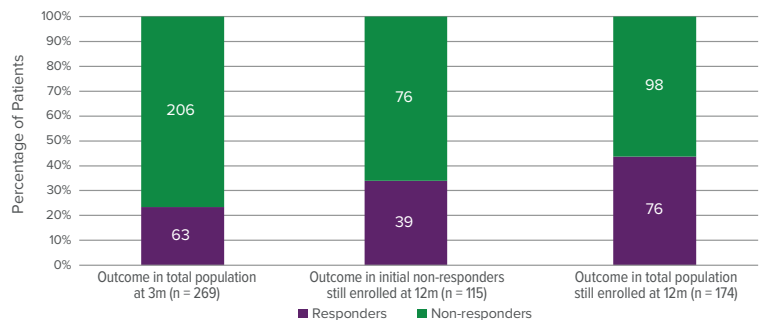
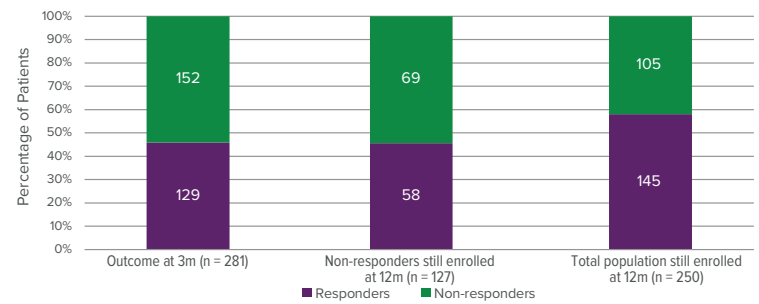


Figure 2. Response rates (≥30% decrease in NPRS) to HCCP in PDPN patients included in the PACE study [1,3] after 3 months, and at 12 months among non-responders at 3 months, and all patients still enrolled at 12 months.



Of the initial non-responders receiving repeat applications and who were still in the trial at 12 months (n=127), 80.2% received at least 4 applications of HCCP, and 45.7% had become responders to HCCP treatment. Among the total population still enrolled at 12 months, 58% of patients could be classified as responders.

Safety/tolerability data from the PACE and STRIDE studies have been published previously [2,3].

Conclusions

Repeat treatment with HCCP over 52 weeks in patients with various types of PNP – which in previous reports has been demonstrated to be well tolerated – provides additional therapeutic benefits in some initial non-responders. As observed across trials, more than one-third of initial non-responders converted into responders with repeated HCCP treatment. Although, after 12 months, the responder rates in patients who did not initially respond to HCCP were approximately 10% lower than in the overall population, the substantial increase in responder rates justifies repeat treatments with HCCP.

References

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Disclosures of Interest

Rainer Freynhagen has been a consultant for Grünenthal.
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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