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Treatment outcomes in patients with post-surgical neuropathic pain: data from a randomized controlled clinical trial comparing high concentration capsaicin patch with pregabalin

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Introduction

Peripheral neuropathic pain (PNP) is a condition for which patient management is challenging since the condition often becomes chronic, with marked long-term reductions in health-related quality of life (QoL), decreased individual productivity, and increased patient and healthcare expenditure. Etiologies range from mechanical and inflammatory diseases to injury and nerve compression. A key pathophysiological mechanism is neuronal hyperexcitability, both within the axon and cell body as well as at the peripheral nociceptors. This allows for single or combined therapies targeting one or more sites within the neuron. Treatments for PNP include systemic and local treatments such as pregabalin or the high concentration 8% capsaicin patch (HCCP). Pregabalin reduces neuronal excitability in the central nervous system, whereas locally applied HCCP rapidly delivers capsaicin into the skin, directly targeting the nociceptor and leading to its defunctionalization.

Post-surgical neuropathic pain (PSNP) is a common yet underdiagnosed PNP condition with a high growing need for treatment of its symptoms. In a recent placebo-controlled trial in patients with post-traumatic neuropathic pain (including patients with PSNP), pregabalin failed to meet the primary endpoint (assessed by a pre-defined change from Baseline to Week 15 on the numeric pain rating scale [NPRS]) but yielded positive results in key secondary endpoints [1]. To date, no direct comparison of the efficacy of HCCP and pregabalin in patients with PSNP have been reported. The ELEVATE study compared the efficacy and safety of HCCP and pregabalin in 559 evaluable patients with PNP of various etiologies [2]. In the present *post-hoc* analysis, we consider a subgroup of patients with PSNP from the ELEVATE study.

Methods

The ELEVATE study was an 8-week, open-label, randomized, multicenter, non-inferiority trial in which eligible patients with PNP were randomly assigned 1:1 to a single treatment with HCCP (179 mg; 8% w/w) or to optimized daily treatment with pregabalin (75 mg capsules). Efficacy assessments included the NPRS, Neuropathic Pain Symptom Index (NPSI), Treatment Satisfaction Questionnaire for Medication (TSQM), QoL using the EQ-5D, Patient Global Impression of Change (PGIC), and Area of Dynamic Mechanical Allodynia (ADMA). The proportion of patients in each arm who achieved a ≥30% decrease in the 'average pain for the past 24 hours' NPRS score from Baseline to Week 8 was assessed (the primary efficacy response). The results presented here pertain to a *post-hoc* analysis using analysis of covariance models and Least Square (LS) means. Baseline observation carried forward (BOCF) analyses were used to account for missing data.

Results

From the ELEVATE study patient cohort, 145 patients had PSNP and were randomized to each group: 78 received treatment with HCCP and 67 received oral pregabalin (Table 1).

Table 1. Demographics and baseline characteristics for the subgroup of patients with post-surgical neuropathic pain (PSNP) in the ELEVATE study (full analysis set).

Parameter	HCCP (N=78)	Pregabalin (N=67)
Gender, n(%)		
Male	30 (38.5)	27 (40.3)
Female	48 (61.5)	40 (59.7)
Ethnicity, n (%)		
White	76 (97.4)	66 (98.5)
Asian	0	1 (1.5)
Other	2 (2.6)	0
Mean (SD) age, years	52.0 (13.4)	50.1 (12.7)
Mean (SD) body mass index, kg/m^2	26.7 (5.9)	27.4 (6.0)
Mean (SD) duration of neuropathic pain diagnosis, years	3.0 (4.6)	1.7 (2.5)

Abbreviations: SD – standard deviation.

The response rates at Week 8 are shown in Figure 1. A reduction in NPRS from Baseline of ≥30% was recorded in a higher proportion of patients treated with HCCP than with pregabalin. Similarly, more patients receiving HCCP than pregabalin were `very much or much improved' according to PGIC scores at Week 8.

Figure 1. Pain relief and patient assessment of improvement after 8 weeks' treatment with HCCP or pregabalin in patients with post-surgical neuropathic pain.

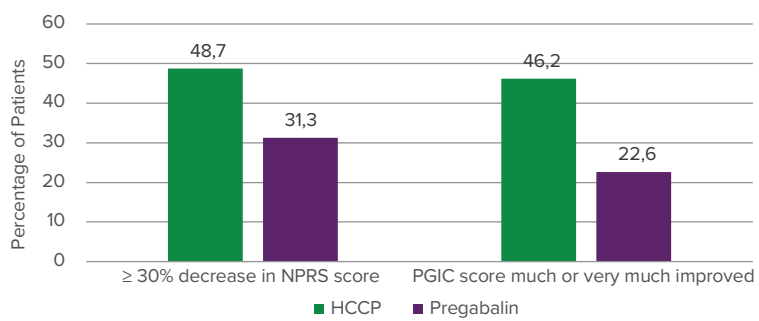

Table 2 includes other key efficacy data. In the HCCP treatment group, by Week 8, the LS mean score for TSQM was higher, the total NPSI score reduction was greater, and the increase in EQ-5D-5L score was greater, than in the pregabalin group. The ADMA was also reduced more in the HCCP group.

Table 2. Changes in efficacy assessment variables after 8 weeks' treatment with HCCP or pregabalin in patients with post-surgical neuropathic pain.

Variable	HCCP	Pregabalin
TSQM global satisfaction (Week 8)	68.7	43.8
Total NPSI score reduction from Baseline (%)	−35.1	−27.0
EQ-5D-5L score increase from Baseline	15.3	4.3
ADMA reduction from Baseline (cm^2)	−78.9	−63.5

Abbreviations: ADMA - Area of Dynamic Mechanical Allodynia; EQ-5D-5L - quality of life assessment; HCCP - high concentration 8% capsaicin patch; NPSI - Neuropathic Pain Symptom Index; TSQM - Treatment Satisfaction Questionnaire for Medication

Conclusions

In patients with PSNP, a single treatment with HCCP compares favorably with daily oral pregabalin at an optimized dose for 8 weeks. This was the case for pain relief, patient assessment of improvement, patient satisfaction, and reduction of ADMA.

References

1. Markman J et al. *J Neurol*. 2018;265:2815–24.
2. Haanpää M et al. *Eur J Pain*. 2016;20:316–28.

Disclosures of Interest

Mayank Gupta 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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