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Treatment outcomes in patients with post-herpetic neuralgia: a controlled trial of capsaicin 8% patch versus oral pregabalin

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Introduction

Despite the availability of a variety of pharmacological interventions, post-herpetic neuralgia (PHN) is a prevalent peripheral neuropathic pain (PNP) condition [1]. It is the most common complication of shingles. In addition to pain, PHN is associated with impaired functionality and quality of life (QoL). One of the established first-line treatments for PHN is pregabalin. High concentration capsaicin patches (HCCP) are a commonly recommended second-line therapy. HCCP 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. The ELEVATE study compared HCCP with oral pregabalin in 559 evaluable patients with PNP [2]. The present report considers the subgroup of patients with PHN from the ELEVATE study.

Methods

The ELEVATE study was an open-label, randomized, multicenter, non-inferiority trial. It was conducted in agreement with ICH GCP, and approvals were obtained from relevant authorities and ethics committees prior to commencement of the trial.

Patients with PHN had pain persisting for at least 6 months after shingles vesicle crusting. Eligible patients were either treatment-naïve to, or – in the investigator's opinion – had previously received inadequate treatment with, gabapentin or pregabalin. The study participants 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 and were followed for 8 weeks.

Patients were assessed at baseline and at predefined times during the study using the following rating scales: Numeric Pain Rating Scale (NPRS); maximum Neuropathic Pain Symptom Inventory (NPSI) subscales [burning (superficial) spontaneous pain, pressing (deep) spontaneous pain, paroxysmal pain, evoked pain, paresthesia/dysesthesia]; Treatment Satisfaction Questionnaire for Medication (TSQM); EuroQol-5D (EQ-5D); Patient Global Impression of Change (PGIC); and Medical Outcomes Study-6 item questionnaire for cognitive function and sleep (MOS). The area of dynamic mechanical allodynia (ADMA) was measured, and adverse events were monitored.

The primary assessment of response was defined as a ≥30% reduction from baseline in the average pain score over a 24-hour period based on the NPRS score. The optimal therapeutic effect was defined as no change in concomitant chronic pain medication, no discontinuation of the trial medication due to lack of efficacy or tolerability prior to the end of the study, ≥30% reduction in NPRS pain score for ≥4 consecutive days between baseline and the end of the study, and no moderate or severe adverse reactions during the stable treatment period. *Post-hoc* analyses with analysis of covariance models were used, with baseline observation carried forward analyses to account for missing data.

Results

A total of 559 patients with PNP were randomized and received treatment in the ELEVATE study. Of these, 136 patients had PHN; 63 were randomized to treatment with HCCP and 73 to oral pregabalin.

As shown in Figure 1, 71.4% of patients were primary endpoint responders (8 weeks) in the HCCP group compared with 76.7% in the pregabalin group (difference: −5.3%, 95% CI: −20.1%, +9.5%). In terms of the optimal response, the numbers were 71.4% versus 63.0%, respectively (difference: +8.4%, 95% CI: −7.3%, +24.1%).

Figure 1. Primary and optimal responses in patients with PHN receiving HCCP or pregabalin after 8 weeks

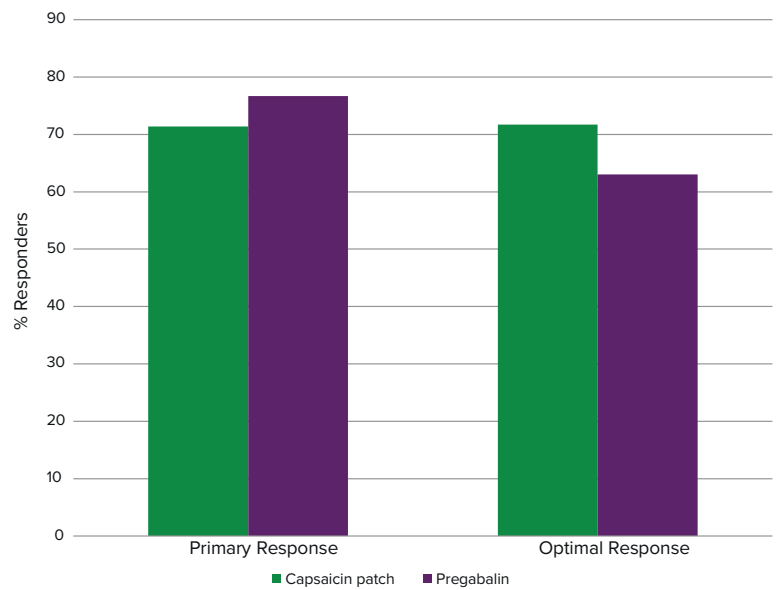

Table 1 presents the key secondary assessment criteria for the two treatment groups. The decrease in total NPSI score, the increase in absolute mean change in QoL (EQ-5D-5L) score, and the percentage of patients with very much or much improvement (PGIC), all showed small favorable responses in the HCCP group. Approximately two-thirds of patients in the HCCP group achieved pain relief within 7 days, versus only one-third of patients receiving pregabalin. TSQM scale outcomes were generally similar between the two treatments, with the exception of the side effects scale which showed better patient satisfaction in the capsaicin treatment group. In total, the percentage of days free from treatment-emergent adverse events was longer in the HCCP group. Furthermore, HCCP provided an optimal therapeutic response in more patients than did pregabalin (Figure 1) and it produced better outcomes on the MOS 6-item questionnaire for cognitive function and sleep, and the response to ADMA (Table 1).

Table 1. Secondary assessment criteria

Parameter	HCCP	Pregabalin	LS mean difference
Total NPSI score - mean (SD) decrease from baseline (%)	−56.4 (40.5)	−47.0 (42.5)	
LS mean TSQM side effects score at Week 8	91.6	78.8	12.8 (95% CI: 5.2, 20.4)
EQ-5D-5L score - absolute mean (SD) change	17.2 (19.7)	13.7 (19.8)	
PGIC - % of patients very much or much improved	69.8	57.7	
MOS scale - mean (SD) change	5.4 (9.9)	0.7 (10.7)	5.7 (95% CI: 2.8, 8.6)
ADMA (cm^2) - mean (SD)change	−162.9 (213.9)	−73.2 (269.7)	
% days free from treatment emergent adverse events - mean (SD)	89.1 (23.0)	74.8 (35.2)	

ADMA - Area of Dynamic Mechanical Allodynia; CI – confidence interval; HCCP – high concentration capsaicin patch; LS - least square; MOS - Medical Outcomes Study; NPSI - Neuropathic Pain Symptom Inventory; PGIC - Patient Global Impression of Change; SD - standard deviation; TSQM - Treatment Satisfaction Questionnaire for Medication

Conclusions

In this subgroup analysis of patients with PNP included in a randomized, controlled clinical trial, treatment outcomes after HCCP compared favorably with those after optimized oral pregabalin. The proportion of patients with a ≥30% reduction in NPRS score (primary response) was similar between treatments, whilst more patients had an optimal response in the HCCP group. In addition, the onset of pain relief was quicker and there was a greater reduction in ADMA. The mean TSQM side effects score was better with HCCP, and fewer patients discontinued treatment because of treatment-related adverse events.

The outcomes of this head-to-head study show that HCCP has comparable efficacy to oral pregabalin, allowing for patient preference and involvement when selecting single or combined therapies for chronic PNP conditions.

References

1. Hadley GR et al. *Curr Pain Headache Rep.* 2016;20:17.
2. Haanpää M et al. *Eur J Pain.* 2016;20:316–28.

Disclosures of Interest

Charles E. Argoff 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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