

---

## ORIGINAL ARTICLE

---

# Treatment of Neuropathic Pain with the Capsaicin 8% Patch: Is Pretreatment with Lidocaine Necessary?

---

Kai-Uwe Kern, MD\*; Walburga Nowack, RN\*; Chris Poole, PhD<sup>†</sup>

\*Centre of Pain Medicine and Palliative Care, Wiesbaden, Germany; <sup>†</sup>Pharmatelligence, Cardiff MediCentre, Cardiff, Wales, UK

■ **Abstract:** The capsaicin 8% patch can effectively treat neuropathic pain, but application can cause discomfort or a burning sensation. Until March 2013, it was recommended that patients be pretreated with a topical anesthetic, for example lidocaine, before capsaicin patch application. However, speculation existed over the need for pretreatment and its effectiveness in alleviating treatment-associated discomfort. This article compares tolerability to and efficacy of the capsaicin patch in pretreated and non-pretreated patients. All patients received a single capsaicin patch application. Pretreated patients received a lidocaine plaster before and intravenous lidocaine and metamizole infusions during capsaicin patch application. Pain levels, assessed using a Numeric

Rating Scale (NRS), were used to determine tolerability and efficacy. All patients (pretreated  $n = 32$ ; non-pretreated  $n = 26$ ) completed 100% of the intended capsaicin patch application duration. At the time of capsaicin patch removal, 69% of pretreated and 88% of non-pretreated patients reported an NRS score increase, which returned to baseline by 6 hours post-treatment. There was no significant difference in mean NRS score between patient groups at any time during or after capsaicin patch treatment. Response was similar between patient groups; capsaicin patch treatment provided rapid and significant pain reductions that were sustained over 12 weeks. The same proportion of pretreated and non-pretreated patients reported willingness to receive retreatment with the capsaicin patch. This analysis shows that the capsaicin 8% patch is generally tolerable, and the small discomfort associated with patch application is short-lived. Lidocaine pretreatment does not have a significant effect on tolerability, efficacy, or patient willingness to receive retreatment. ■

**Key Words:** capsaicin, nerve pain, neuralgia, nociceptors, peripheral nervous system, topical, tolerability, lidocaine pretreatment

Address correspondence and reprint requests to: Kai-Uwe Kern, MD, Institute of Pain Medicine, Pain Practice, Sonnenberger Str. 68, 65193, Wiesbaden, Germany. E-mail: dr.kern@schmerzpraxis-wiesbaden.de

Disclosures: Dr Kern is a consultant or presenter for Astellas, Berlin Chemie, Boehringer Ingelheim, Betapharm, Grünenthal, Lilly, Medi Bayreuth, and Mundipharma and received LIIRA Grant support for clinical research from Pfizer. Pharmatelligence has received consultancy fees from Astellas, Grünenthal, and Pfizer. Dr Poole has also consulted for Astellas. Kai-Uwe Kern is no longer an employee at the Centre of Pain Medicine and Palliative Care and now works at the Institute of Pain Medicine, Pain Practice. Chris Poole is no longer an employee at Pharmatelligence and now works at Cardiff University.

Submitted: April 16, 2013; Revision accepted: September 16, 2013  
DOI: 10.1111/papr.12143

---

© 2013 The Authors. *Pain Practice* published by Wiley Periodicals, Inc. on behalf of World Institute of Pain.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

1530-7085/13/\$15.00

*Pain Practice*, Volume 14, Issue 2, 2014 E42–E50

## INTRODUCTION

Neuropathic pain (NP), a chronic and disabling condition, affects up to 8% of the European population.<sup>1–3</sup> Treatments include tricyclic antidepressants, opioids, anticonvulsants, and topical capsaicin or lidocaine creams.<sup>4,5</sup> Many of these NP medications have limited efficacy, with typically fewer than 50% of patients

achieving satisfactory pain relief.<sup>4</sup> Additionally, cumbersome treatment regimens and unwanted systemic side effects are commonly associated with many medications, often resulting in patient intolerance to treatment and leading to poor compliance.<sup>6</sup>

The capsaicin 8% patch (QUTENZA™) is indicated in Europe for the treatment of peripheral NP in nondiabetic adults either alone or in combination with other medicinal products for pain. Capsaicin causes excitation of the Transient Receptor Potential Vanilloid 1 (TRPV1) channels, expressed on nociceptors, leading to the generation of action potentials and a burning sensation in the skin.<sup>7</sup> However, administration of capsaicin at a high concentration leads to constant overstimulation of the nociceptors and results in a reversible reduction in epidermal nerve fiber density and defunctionalization of the nociceptors. The overall outcome of this is a reduction in NP.<sup>8–11</sup> Treatment with the capsaicin 8% patch is not associated with any systemic side effects, and a single application can provide significant relief from NP for up to 3 months.<sup>12–15</sup>

Due to the mechanism of action of capsaicin, patients treated with the capsaicin 8% patch may experience a burning sensation during application.<sup>7,11</sup> Until recently, it was therefore recommended that, to alleviate any discomfort, patients receive pretreatment with a topical anesthetic, such as lidocaine or EMLA®, before patch application. However, there was speculation regarding the utility of topical anesthetics to block capsaicin-related discomfort and, in March 2013, updates were made to the recommendations for pretreatment to state that the treatment area may be pretreated with a topical anesthetic or the patient might be administered an oral analgesic prior to patch application.<sup>16</sup> Amide-type anesthetics (such as lidocaine) prevent nerve impulse transmission through inhibition of sodium ion channels and so reduce the transmission of pain.<sup>17</sup> However, these sodium channels act independently of the TRPV1 receptors at peripheral nerve terminals. Consequently, TRPV1 can induce axonal depolarization and defunctionalization even in the presence of sodium channel blockade.<sup>18,19</sup>

At the Centre of Pain Medicine and Palliative Care in Wiesbaden, Germany, the capsaicin 8% patch is routinely used to treat a variety of patients with NP. Initially, the capsaicin 8% patch was largely used to treat those patients who had been experiencing NP for a long time and had not responded well, or at all, to other medications. At this time, the original recommendations

with regard to pretreatment were followed and all patients received pretreatment with lidocaine before application of the capsaicin 8% patch. As experience with the patch was gained by healthcare professionals at the clinic and positive effects of the treatment were observed, the capsaicin 8% patch was offered to new patients who were at an earlier point in their disease progression. The experience gained also affected how the healthcare professionals chose to manage treatment-associated discomfort and raised questions around the necessity of pretreatment with lidocaine, ultimately resulting in the discontinuation of its routine use in this clinic.

Here, the authors report an analysis of the tolerability and efficacy of treatment with the capsaicin 8% patch in patients at the clinic in Wiesbaden, comparing the experience of patients who did and did not receive lidocaine pretreatment prior to capsaicin 8% patch therapy.

## METHODS

### Patients

All patients diagnosed with an NP condition and receiving treatment with the capsaicin 8% patch between May 2010 and May 2011 at the Centre of Pain Medicine and Palliative Care, Wiesbaden, Germany were included in the analysis. Ethical approval for this retrospective analysis was granted on December 13, 2011 from the Ethik-Kommission bei der Landesärztekammer Hessen. As this was a retrospective analysis, informed consent was not required and all treatments and assessments were consistent with the usual standard of care.

### Procedure

The application procedure for the capsaicin patch was carried out as described previously.<sup>20</sup> Following pretreatment, as appropriate, the capsaicin 8% patch was applied for 30 minutes to the feet and for 60 minutes to all other areas of the body.

**Pretreatment.** Patients receiving pretreatment were asked to apply a lidocaine patch (Versatis®; Grünenthal, Germany) 2 hours prior to capsaicin 8% patch application. Pretreated patients were provided with an intravenous infusion of lidocaine, 80 mg (Braun, Germany) for 1 hour during patch application, and

the majority were also provided with an infusion of metamizole, 1 g (Lichtenstein, Germany) during capsaicin patch application. For those patients treated on the feet, the lidocaine infusion continued for 30 minutes after removal of the capsaicin patch. A few patients received lidocaine and metamizole infusions without lidocaine patch application. Patients not receiving pretreatment did not receive cleansing of the skin prior to capsaicin patch application as this was not necessary.

### Management of Treatment-related Discomfort

Treatment-related discomfort was monitored during and after the application procedure. Patients who experienced discomfort during patch application could receive metamizole 1 g, and if further analgesia was required, piritramide 3.75 to 30 mg (Janssen-Cilag, Germany). After the capsaicin patch had been removed, patients received localized cooling to alleviate any continued discomfort.

### Pain Level Assessment

Pain or discomfort pre- and postcapsaicin patch application was assessed using a Numeric Rating Scale (NRS), where patients were asked to score their pain on an integer scale of 0 to 10, with 0 meaning “no pain” and 10 representing “worst imaginable pain.” Using pain diaries, patients were asked to assess their pain for the week prior to treatment, immediately prior to the initiation of treatment, and at 0.5, 1, 6, 12, and 24 hours and 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30, and 90 days after capsaicin 8% patch application.

### Tolerability

Tolerability was assessed by the number of patients who completed the intended duration of capsaicin 8% patch application, by the change in pain score at the time of patch removal and up to 24 hours postpatch removal, and by the requirement for additional analgesics. The NRS score immediately prior to the initiation of treatment was used as the baseline in analysis of change in pain score.

### Efficacy

Efficacy was assessed by the absolute change in NRS score from baseline, the percentage change in NRS

score, and the proportion of responders, classified as patients who exhibit  $\geq 30\%$  reduction from baseline in pain score up to 90 days post-treatment. When assessing efficacy, the mean NRS score for the week prior to treatment was used as the baseline pain score.

### Statistical Analysis

Differences in baseline characteristics were tested appropriately to their respective distributions. Given the ordinal properties of the NRS scale, between-group (pretreated and non-pretreated patients) differences in change in absolute pain score from baseline were first tested at each timepoint (24 hours and 30 and 90 days post-treatment) with the nonparametric Mann–Whitney *U*-test, then collectively using repeated-measures ordinal logistic general estimating equation (GEE) modeling with multinomial distribution with a cumulative logit link function. As percentage change in pain exhibited an approximately normal distribution and pseudo-scale properties, initial between-group comparisons at the fixed timepoints were made using the independent samples Student’s *t*-test, followed by repeated-measures linear GEE modeling, with normal distribution and an identity link function. Measurement time and pretreatment subgroup were modeled as fixed factors in all analyses. SPSS v20 (IBM Corp., Armonk, NY, USA) statistical software was used for all inferential testing. The threshold parameter significance was set at  $P \leq 0.05$  for all tests.

### Retreatment

At 30 and 90 days post-treatment, patients were asked to record in their pain diary whether they would be happy to receive retreatment with the capsaicin 8% patch. From 10 weeks after initial treatment, patients could request retreatment with the capsaicin 8% patch if their pain had returned to around 80% of the baseline level.

## RESULTS

### Patients

Between May 2010 and May 2011, 58 patients received a total of 82 capsaicin 8% patch treatments at the Centre of Pain Medicine and Palliative Care, Wiesbaden, Germany. Of these patients, 41 received 1 treatment, 12 patients were treated twice, 4 patients received three treatments, and 1 patient received five

treatments. Only data from the first capsaicin 8% patch treatment received by the 58 patients are included in the analyses reported here. Of these first treatments, 32 patients received pretreatment and 26 received no pretreatment. Among the pretreated patients, 21 received a lidocaine patch plus infusions of lidocaine and metamizole, 8 received only infusions of lidocaine and metamizole, while 3 patients received a lidocaine patch and a lidocaine infusion.

Pretreatment was routinely carried out as part of the capsaicin 8% patch treatment procedure for the first 5 months of using the therapy at the center (between May and October 2010). In November 2010, the decision was made to utilize the capsaicin 8% patch without pretreatment where possible. This was a clinical decision based on the experience gained of the treatment procedure and after hearing the opinion of other experienced users of the capsaicin 8% patch who had routinely provided pretreatment. It was felt that it would be beneficial to remove the lengthy pretreatment step if possible and that this would not be detrimental to the patient or efficacy of the treatment. After the pretreatment step was removed, it soon became apparent that pretreatment is not necessary in most cases.

A comparison at baseline showed that pretreated and non-pretreated patients were similar in most regards,

**Table 1. Baseline Characteristics of All Patients**

	Non-pretreated (n = 26)	Pretreated (n = 32)	P value
Male, n (%)	10 (38)	16 (50)	0.380
Age, years (SD)	64.9 (15.3)	61.4 (14.8)	0.376
Pain duration, years (SD)	2.2 (2.2)	5.5 (3.6)	<0.001
Application time, n (%)			
30 minutes	1 (4)	7 (22)	—
60 minutes	25 (96)	25 (78)	0.110
NRS score prior to treatment (SD)	4.8 (2.0)	5.3 (2.6)	0.416
NP diagnosis, n (%)			
Postherpetic neuralgia	15 (58)	10 (31)	—
Mononeuropathy	4 (15)	6 (19)	—
Polyneuropathy	1 (4)	3 (9)	—
Postsurgical/post-trauma	4 (15)	5 (16)	—
FBSS/postdiscectomy	0	4 (13)	—
Other	2 (8)	4 (13)	0.250
Concomitant medications for pain, n (%)			
Any	23 (88)	31 (97)	0.209
Opioids	13 (50)	22 (69)	0.147
Anticonvulsants	9 (35)	18 (56)	0.100
Antidepressants	6 (23)	2 (6)	0.065
Other	14 (54)	11 (34)	0.136
Mean number of concomitant medications for pain taken by each patient (SD)	1.8 (1.4)	1.8 (0.9)	0.913

FBSS, failed back surgery syndrome; SD, standard deviation.

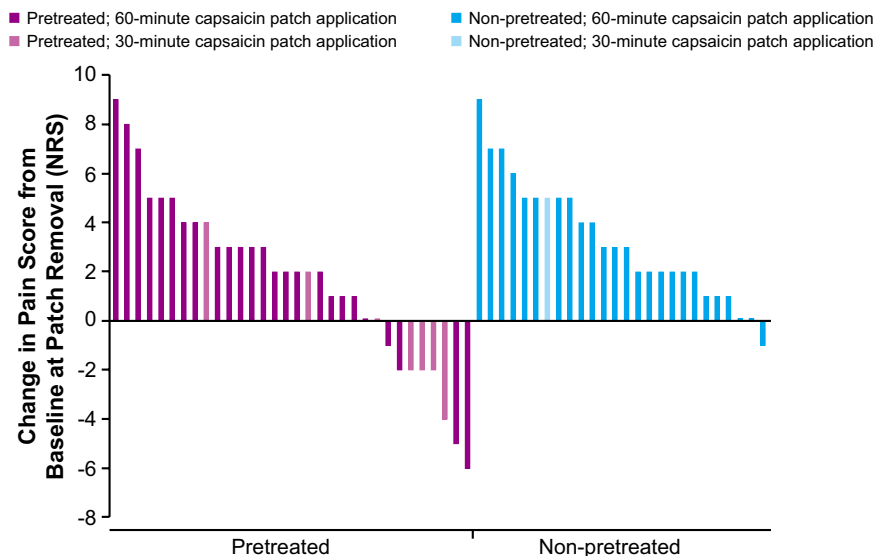
except for the mean duration of NP, which was significantly greater in the population of pretreated patients compared with non-pretreated patients (Table 1).

### Tolerability

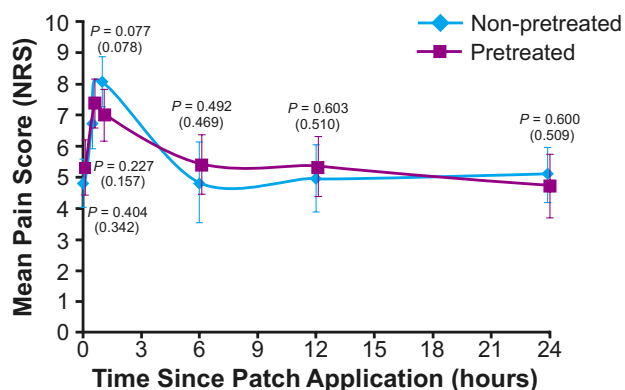
All patients completed 100% of the intended capsaicin 8% patch application time. At the time of capsaicin 8% removal, 22 (69%) pretreated patients and 23 (88%) non-pretreated patients reported an increase in NRS compared with NRS immediately prior to initiation of treatment, while 8 (25%) pretreated patients and 1 (4%) non-pretreated patient reported a decrease in NRS compared with NRS immediately prior to initiation of treatment (Figure 1). Of those patients reporting a decrease in NRS, 4 (44%) had received a 30-minute capsaicin patch application. A moderate increase in NRS (increase of > 5) was reported in 3 (9%) patients who received pretreatment and 4 (15%) patients who did not (Figure 1).

During treatment, there was an increase in mean NRS score in both pretreated and non-pretreated patients, but this rapidly declined and by 6 hours after capsaicin 8% patch application, NRS scores had returned to baseline levels in both groups (Figure 2). There was no significant difference in mean NRS score between non-pretreated and pretreated patients at any time during or immediately after the treatment period, up to 24 hours postapplication. As analgesic responses are often not distributed equally around the mean, the data were analyzed using both parametric and nonparametric statistical methods. The same result was observed when using either test (Figure 2). This was corroborated by ordinal logistic GEE that revealed no significant parameter effect for pretreatment allocation ( $P = 0.508$ ).

In total, 34 patients requested additional analgesia during application of the capsaicin 8% patch due to treatment-related discomfort. Twenty-two patients (65%) received only nonopioid analgesia (either metamizole or ketoprofen), 3 (9%) received piritramide only, while 9 (26%) received both nonopioid and opioid analgesia. Despite the slightly higher increase in NRS among patients who did not receive pretreatment compared with those who did, there was no significant difference in nonopioid treatment. However, significantly, more pretreated patients than non-pretreated patients received piritramide during capsaicin 8% patch treatment (31% vs. 8%;  $P = 0.028$ ; Table 2).



**Figure 1.** Change in pain score from baseline at removal of capsaicin 8% patch. Data for individual patients receiving lidocaine pretreatment ( $n = 32$ ) and receiving no pretreatment ( $n = 26$ ) are shown, ordered by size of change in Numeric Rating Scale (NRS) score from baseline.



**Figure 2.** Mean pain scores ( $\pm$ SD) for pretreated and non-pretreated patients during the first 24 hours after capsaicin 8% patch treatment.  $P$  values for pretreated ( $n = 32$ ) vs. non-pretreated ( $n = 26$ ) patients were calculated using a  $t$ -test for equality of means, not assuming equal variance, and using the Mann-Whitney  $U$ -test that compares ranks and is therefore not affected by the distribution of the dependent variable.  $P$  values from the Mann-Whitney  $U$ -test are presented in brackets.

Tolerability was also assessed in patients grouped according to their baseline NRS score, using the mean NRS for the week prior to treatment. The general trend appeared to be for patients with a higher baseline NRS score (7 to 10) to exhibit a decrease in NRS score from baseline at 0.5, 1, 6, and 12 hours after application of

the capsaicin 8% patch (Figure S1). In patients with a lower baseline pain score (NRS 3 to 6), it was more common to see an increase in NRS from baseline at 30 and 60 minutes postpatch application and then a reduction at 6 and 12 hours postpatch application, returning to near or below baseline levels (Figure S1). There was no apparent difference between patients who received pretreatment and those who did not receive pretreatment.

**Adverse Events.** In general, adverse events were limited to application site events, including erythema and treatment-related discomfort, which were mild and self-limited. One patient developed an allergic reaction distant from the application site, which required a physician consultation, and led to sleep disturbance the same night, 3 other patients required a physician consultation during treatment due to treatment-related discomfort, and 3 further patients reported sleep disturbance during the first night after treatment.

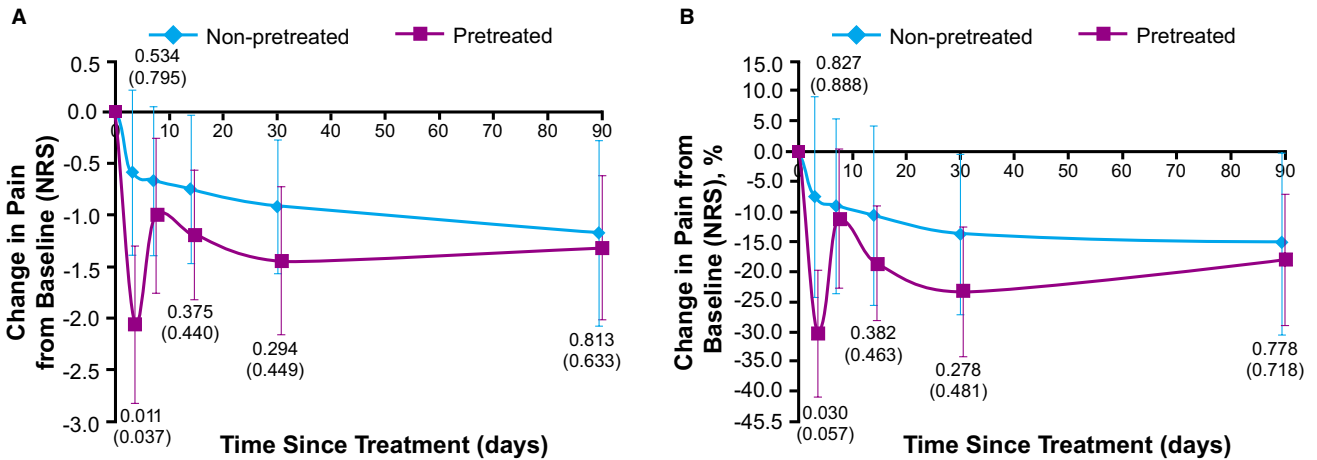
### Efficacy

Following capsaicin 8% patch treatment, a reduction in NRS score of  $\geq 30\%$  was seen in 31% of pretreated

**Table 2. Requirement for Additional Pain Medication during Capsaicin 8% Patch Treatment**

	Non-pretreated, $n$ (%)	Pretreated, $n$ (%)	$P$ value*	Odds ratio	95% CI
Nonopioid pain medication	15 (58)	16 (50)	0.559	0.733	0.26 to 2.08
Opioid pain medication (pir tramide)	2 (8)	10 (31)	0.028	5.455	1.07 to 27.69

\*Pretreated vs. non-pretreated; calculated using chi-squared test. CI, confidence interval.



**Figure 3.** Change in pain score from baseline in pretreated and non-pretreated patients. (A) Change in absolute Numeric Rating Scale (NRS) score and (B) percentage change in NRS score from baseline (mean pain score during the week before treatment) is shown. *P* values for pretreated (*n* = 32) vs. non-pretreated (*n* = 24) patients were calculated using a t-test for equality of means, not assuming equal variance, and using the Mann–Whitney *U*-test that compares ranks and is therefore not affected by the distribution of the dependent variable. *P* values from the Mann–Whitney *U*-test are presented in brackets.

patients and 26% of non-pretreated patients after 30 days, and in 38% of pretreated patients and 30% of non-pretreated patients after 90 days. The difference between pretreated and non-pretreated patients was not significant at either timepoint (*P* = 0.678 and *P* = 0.587, respectively).

The pain reductions observed were rapid and sustained over 90 days (Figure 3). At initial timepoints, pretreated patients exhibited a greater reduction in pain score from baseline than non-pretreated patients. From Day 7 to Day 90, there was no difference between the

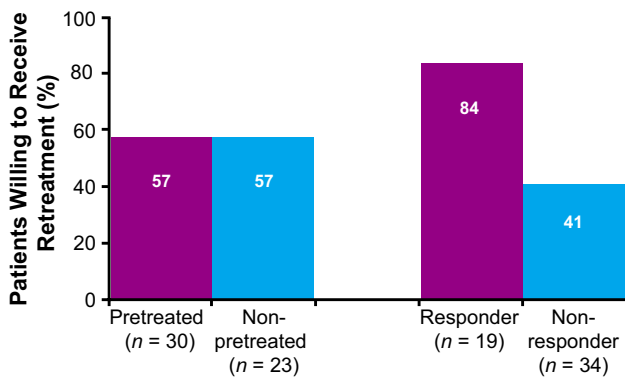
two groups (Figure 3). Use of parametric tests demonstrated a significant difference between percentage reduction from baseline in NRS score at Day 3 post-treatment (Figure 3B). However, the nonparametric analysis found no significant difference at this timepoint. At all other timepoints, there was no significant difference regardless of the test used. These findings were corroborated by ordinal logistic GEE of absolute change in pain score and linear GEE of percentage change in pain score; in both instances, pretreatment allocation was not a significant predictor (*P* = 0.273 and *P* = 0.244, respectively).

### Retreatment

Thirty and 90 days after treatment, there was no difference between the number of pretreated and non-pretreated patients who would be happy to receive capsaicin 8% patch retreatment if and when necessary (Figure 4). A greater proportion of responders (patients with a ≥ 30% decrease in NRS from baseline) than nonresponders at 90 days stated that they would be willing to receive retreatment (84% vs. 41%; *P* = 0.002).

### DISCUSSION

Observations in this real-life clinical setting suggest that the tolerability of capsaicin 8% patch application is similar regardless of whether patients have received



**Figure 4.** Proportion of patients stating that they would be happy to receive capsaicin 8% patch retreatment when necessary. Patients were asked to record if they would be willing to receive capsaicin 8% patch retreatment 90 days after initial treatment. The proportion of pretreated and non-pretreated patients and the proportion of responders, classified as those patients with ≥ 30% decrease in NRS from baseline, and nonresponders willing to receive retreatment are shown.

lidocaine pretreatment or not. In particular, comparing patients receiving or not receiving pretreatment, a similar number requested pain relief with metamizole during capsaicin 8% patch application. Moreover, whether or not a patient had received pretreatment had no effect on the willingness of patients to receive retreatment with the capsaicin 8% patch, with the majority of patients stating they would be happy to receive retreatment when necessary. Interestingly, the data suggest that patients with more pain at baseline may tolerate application of the capsaicin 8% patch better than patients with less pain at baseline. It may be that patients who generally experience a higher level of NP do not find that the discomfort caused by the capsaicin 8% patch is strong enough to cause them more pain than they already experience, while patients with a lower baseline level of pain may be more sensitive to other stimuli that can cause discomfort.

Whether or not patients received pretreatment also did not have any effect on the efficacy of capsaicin 8% patch treatment. Although pretreated patients displayed a greater reduction in pain than non-pretreated patients initially, there was no significant difference in pain reduction between the patient groups at timepoints from Day 7 through to Day 90. Thirty days after treatment, 31% of pretreated patients and 26% of non-pretreated patients had a reduction in NRS score of  $\geq 30\%$  compared with baseline. Due to the way in which we collected our patients' data, it is not possible to carry out a direct comparison between efficacy of the capsaicin patch in our patients and data seen in the clinical trials, in which patients with postherpetic neuralgia received treatment with the capsaicin 8% patch. Nonetheless, our data may be considered to be comparable to those in the clinical trials, in which 42% to 46% of patients achieved a reduction of  $\geq 30\%$  in pain score during Weeks 2 to 8 compared with baseline.<sup>12,14</sup> While we chose to report response to capsaicin 8% patch treatment by analyzing the mean change from baseline in pain score to allow this informal comparison with clinical trial data, we note that analgesic response is not normally distributed around the mean, raising possible concerns regarding the use of parametric statistical methods. We therefore carried out additional analysis of the mean changes in pain score using nonparametric tests that compared differences in ranks of pain scores. This analysis demonstrated that the data are similar regardless of the technique used and supports the validity of the parametric analysis. This is in line with experience that nonparametric methods are normally

consistent with parametric methods, unless the distribution of data is very substantially skewed.<sup>21</sup>

It is interesting to note that of 8 pretreated patients showing a decrease from baseline in NRS at the time of patch removal, 4 had received a 30-minute treatment. These data are perhaps not that unexpected, as it is likely that the effects of the pretreatment medication on the patient's NP are still being felt after 30 minutes, but the effects will subside by 60 minutes. Moreover, we and others have noted that the onset of treatment-related discomfort usually occurs around 30 minutes after application of the capsaicin 8% patch.<sup>22</sup>

The major disadvantage of this study is its retrospective nature and the potential for bias to have been introduced into the study. It could be argued that the analysis presented in this article was carried out to confirm an assumption already made when clinical practice was changed to stop pretreatment; that assumption being that pretreatment was not usually necessary. However, while we did feel at the time of changing clinical practice that pretreatment may be an unnecessary step, it was only after removal of the pretreatment step and observing patients' responses that we decided that pretreatment was not necessary. Throughout the entire time period covered in the current analysis, the assessment measures remained the same for all patients, who were asked to score their pain on a rating of 0 to 10 at the same predefined timepoints post-treatment. All patients used the same 11-point pain rating scale and recorded their score in pain diaries. The retrospective analysis we present here is based on pain scores retrieved using these assessments, and therefore, the outcomes are largely independent of any predrawn conclusion.

The results of the analysis presented here are likely to have been affected in part by the timeframe in which the data were collected. Our analysis covers the first year after which we started treating patients with the capsaicin 8% patch and discontinuation of the routine use of pretreatment occurred as we became more experienced with use of the patch. Thus, in general, patients receiving pretreatment were treated by staff less experienced in capsaicin patch use than those not receiving pretreatment. This factor is likely to account for the significantly greater number of pretreated than non-pretreated patients requesting treatment with opioid pain medication during capsaicin 8% patch application. Other limitations of this study include the small number of patients included within the analysis and the fact that the results are from a single center.

Nonetheless, these limitations do not affect the major conclusion of our analysis, namely that treatment of patients with the capsaicin 8% patch without analgesic pretreatment is well tolerated by the majority of patients. Indeed, we believe that improvements in the experience of patient management and treatment procedures may actually have more effect on the tolerability of capsaicin 8% patch treatment than lidocaine pretreatment. The importance of patient management to ensure good tolerability of capsaicin 8% patch treatment has been described in detail previously by a group of experienced users.<sup>20</sup> Our positive experience of treating patients with the capsaicin 8% patch without using lidocaine pretreatment means that we continue to do this routinely, with over 150 treatments carried out to date.

The manner in which the data were collected is also likely to account for the significant difference in mean duration of NP between pretreated and non-pretreated patients. In general, when the capsaicin patch became available for the treatment of peripheral NP those patients with long-standing NP that was not effectively controlled by other medications were the first to receive this new treatment.

There are practical benefits to not pretreating patients before application of the capsaicin 8% patch. These include a reduction in total treatment time, which would be advantageous to both patients and healthcare professionals, and a potential cost benefit, resulting from removal of the cost of the pretreatment medication(s). Further studies are warranted to investigate these benefits further.

An additional point to note is that in March 2013, updates were made to the recommendations for pretreatment before capsaicin 8% patch application. The label now states that the treatment area may be pretreated with a topical anesthetic or the patient might be administered an oral analgesic prior to patch application. The findings from this analysis align with these updates in suggesting that pretreatment with a topical anesthetic may not be necessary when administering the capsaicin 8% patch.

In conclusion, the data presented here from the Centre of Pain Medicine and Palliative Care in Wiesbaden indicate that the small increase in discomfort that is seen in most patients during capsaicin 8% patch application is short-lived and tolerable, regardless of whether the patient has received pretreatment with lidocaine or not, and it neither deters patients from accepting retreatment nor does it affect efficacy.

## ACKNOWLEDGMENTS

Editorial assistance was provided by Adelphi Communications Ltd, supported by Astellas Pharma Europe Ltd.

## REFERENCES

1. Bouhassira D, Lantéri-Minet M, Attal N, Laurent B, Touboul C. Prevalence of chronic pain with neuropathic characteristics in the general population. *Pain*. 2008;136:380–387.
2. Mailis Gagnon A, Furlan A, Lakha SF, Yegneswaran B. Systematic review of the prevalence of neuropathic pain. *Eur J Pain*. 2007;11(Suppl. 1):S202–S203 (Abstract 457).
3. Torrance N, Smith BH, Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. *J Pain*. 2006;7:281–289.
4. O'Connor AB, Dworkin RH. Treatment of neuropathic pain: an overview of recent guidelines. *Am J Med*. 2009;122(10 Suppl.):S22–S32.
5. Stillman M. Clinical approach to patients with neuropathic pain. *Cleve Clin J Med*. 2006;73:726–739.
6. Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc*. 2010;85(3 Suppl.):S3–S14.
7. Wallace M, Pappagallo M. Qutenza®: a capsaicin 8% patch for the management of postherpetic neuralgia. *Expert Rev Neurother*. 2011;11:15–27.
8. Anand P, Bley K. Topical capsaicin for pain management: therapeutic potential and mechanisms of action of the new high-concentration capsaicin 8% patch. *Br J Anaesth*. 2011;107:490–502.
9. Kennedy WR, Vanhove GF, Lu SP, et al. A randomized, controlled, open-label study of the long-term effects of NGX-4010, a high-concentration capsaicin patch, on epidermal nerve fiber density and sensory function in healthy volunteers. *J Pain*. 2010;11:579–587.
10. Malmberg AB, Mizisin AP, Calcutt NA, et al. Reduced heat sensitivity and epidermal nerve fiber immunostaining following single applications of a high-concentration capsaicin patch. *Pain*. 2004;111:360–367.
11. McCormack PL. Capsaicin dermal patch: in non-diabetic peripheral neuropathic pain. *Drugs*. 2010;70:1831–1842.
12. Backonja M, Wallace MS, Blonsky ER, et al. NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia: a randomised, double-blind study. *Lancet Neurol*. 2008;7:1106–1112.
13. Backonja MM, Malan TP, Vanhove GF, Tobias JK. NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia: a randomized, double-blind, controlled study with an open-label extension. *Pain Med*. 2010;11:600–608.
14. Irving GA, Backonja MM, Duntzman E, et al. A multicenter, randomized, double-blind, controlled study of



NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia. *Pain Med.* 2011;12:99–109.

15. Simpson DM, Brown S, Tobias J. Controlled trial of high-concentration capsaicin patch for treatment of painful HIV neuropathy. *Neurology.* 2008;70:2305–2313.

16. Astellas Pharma Europe Ltd. *Summary of Product Characteristics: Qutenza 179 mg Cutaneous Patch.* London, UK: European Medicines Agency; 2013 (cited 31 July 2013); Available from: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/000909/WC500040453.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000909/WC500040453.pdf).

17. Medicines and Healthcare product Regulatory Agency (MHRA). *LMX 4 lidocaine 4% w/w cream: PL 20685/0034.* London, UK: MHRA; 2007 [cited 31 July 2013]; Available from: [www.mhra.gov.uk/home/groups/l-unit1/documents/web\\_siteresources/con2033763.pdf](http://www.mhra.gov.uk/home/groups/l-unit1/documents/web_siteresources/con2033763.pdf).

18. Craft RM, Porreca F. Tetracaine attenuates irritancy without attenuating desensitization produced by intravesical resiniferatoxin in the rat. *Pain.* 1994;57:351–359.

19. Lam VY, Wallace M, Schulteis G. Effects of lidocaine patch on intradermal capsaicin-induced pain: a double-blind, controlled trial. *J Pain.* 2011;12:323–330.

20. England J, Wagner T, Kern KU, Roth-Daniek A, Sell A. The capsaicin 8% patch for peripheral neuropathic pain. *Br J Nurs.* 2011;20:926–931.

21. Tanizaki H. Power comparison of non-parametric tests: small-sample properties from Monte Carlo experiments. *J Appl Stat.* 1997;24:603–632.

22. Wagner T, Roth-Daniek A, Sell A, England J, Kern K-U. Capsaicin 8% patch for peripheral neuropathic pain: review of treatment best practice from ‘real-world’ clinical experience. *Pain Manag.* 2012;2:239–250.

## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Mean change in pain score from baseline to 24 hours in pretreated and non-pretreated patients. Changes in mean absolute Numeric Rating Scale (NRS) score from baseline (NRS score immediately prior to capsaicin 8% patch treatment) to times during the first 24 hours following patch application were determined for patients grouped according to mean baseline NRS in the week before treatment with the capsaicin 8% patch.