

Duration of treatment response to QUTENZA™ (NGX-4010), a high-concentration capsaicin patch, in patients with post-herpetic neuralgia

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BACKGROUND

- Traditional therapies for post-herpetic neuralgia (PHN) frequently provide incomplete pain relief and their use is often limited by side effects.¹
- The observation that many patients with PHN demonstrate hypersensitivity of peripheral nociceptors that express Transient Receptor Potential Vanilloid 1 (TRPV1)² has led to the emergence of TRPV1 as a promising therapeutic target.
- Capsaicin, a potent agonist of the TRPV1 receptor, can reversibly defunctionalise TRPV1-expressing small-diameter sensory afferent fibres resulting in an inhibition of pain transmission.^{3,4}
- NGX-4010 (QUTENZA™) is an 8% capsaicin patch indicated in Europe to treat peripheral neuropathic pain in non-diabetic adults, either alone or in combination with other medicinal products for pain.
- A single application of NGX-4010 provides rapid and prolonged pain relief for up to 3 months in patients with PHN.^{5,6}
- Analyses were performed on efficacy data from a 40-week open-label extension of a 12-week double-blind study to evaluate duration of response to NGX-4010 in patients with PHN.

METHODS

STUDY DESIGN

- This Phase II/III study consisted of two phases in which patients with PHN were randomised in a 12-week, double-blind, controlled phase to receive an application of NGX-4010 (n=222) or a low-concentration capsaicin (0.04% w/w) control patch (n=77) for 30, 60 or 90 minutes.
- This was followed by a 40-week, open-label extension phase during which patients could receive up to three 60-minute NGX-4010 treatments at least 12 weeks apart, as warranted by the return of pain.

PATIENTS

- Eligible patients had moderate-to-severe neuropathic pain secondary to PHN ≥6 months after herpes zoster lesion healing and a Numeric Pain Rating Scale (NPRS) score of 3–9 (inclusive).
- Patients taking chronic neuropathic pain medications had to be on a stable dose prior to and during study participation. Topical pain medications were not permitted.

ASSESSMENTS

- Patients recorded their average pain for the past 24 hours daily at 21:00 hours using the 11-point NPRS.
- Responders were defined as those with two consecutive weekly NPRS score reductions from baseline of ≥30% within 6 weeks after their first (double-blind or open-label) NGX-4010 treatment. NPRS scores obtained on or after the second NGX-4010 treatment were not used.
- Response duration was defined as the number of weeks between the first (double-blind or open-label) NGX-4010 treatment and relapse.
- Relapse was defined as two consecutive weekly pain reductions of <20% or one pain reduction of <20% followed by study drop-out.
- Kaplan–Meier survival estimates were calculated for duration of response. Durations of response for patients who had not relapsed were censored by the date of withdrawal from the study or second NGX-4010 treatment, whichever occurred first.
- The effect of the following variables on response duration was explored using a log-rank test and a proportional hazard model:
 - Age
 - PHN duration
 - Baseline pain score
 - Size of the treatment area
 - Maximum pain increase on the treatment day

- Treatment duration
- Gender
- Pain reduction at Week 2
- Use of concomitant neuropathic pain medication (defined as use of non-selective serotonin reuptake inhibitor antidepressants, anticonvulsants or opioids on Day -1 for at least 7 consecutive days).

RESULTS

- A total of 282 patients received NGX-4010 in the two phases of the study. Of these:
 - Two hundred and twenty-two patients were randomised to receive NGX-4010 in the double-blind phase
 - Sixty patients were randomised to receive control in the double-blind phase and subsequently received an open-label NGX-4010 treatment
 - A total of 123 patients (44%) responded (≥30% pain reduction for 2 consecutive weeks occurring within 6 weeks after their first NGX-4010 treatment).
- Table 1 summarises patient demographics and clinical characteristics of all patients who received NGX-4010.

Table 1: Baseline patient demographics and clinical characteristics (all patients receiving NGX-4010)

Characteristic	Responders (n=123)	Non-responders (n=159)	Total (n=282)
Mean age, years – SD	69.6 – 10.7	73.0 – 9.1	72.0 – 9.9
Female, n (%)	68 (55)	72 (45)	140 (50)
Mean duration of PHN, years – SD [Range]	3.3 – 4.4 [0.3–32.3]	4.0 – 4.7 [0.5–34.2]	3.7 – 4.6 [0.3–34.2]
Mean baseline* average pain for the past 24 hours – SD	5.2 – 1.6	5.9 – 1.5	5.6 – 1.6
On concomitant pain medication [†] , n (%)	62 (50)	83 (52)	145 (51)
Mean size of painful area, cm ² – SD	339 – 231	401 – 250	374 – 243
Mean maximal increase in pain score on the treatment day – SD	2.0 – 3.0	2.0 – 2.7	2.0 – 2.8

PHN=post-herpetic neuralgia; SD=standard deviation.
*Baseline pain level was defined as the mean of all available non-biased screening Numeric Pain Rating Scale scores in that category.
[†]A patient was defined as being on concomitant pain medication if pain medication started prior to the day of treatment, continued on the day of treatment, and was taken for at least 7 days.

Figure 1: Kaplan–Meier estimate of time to relapse.

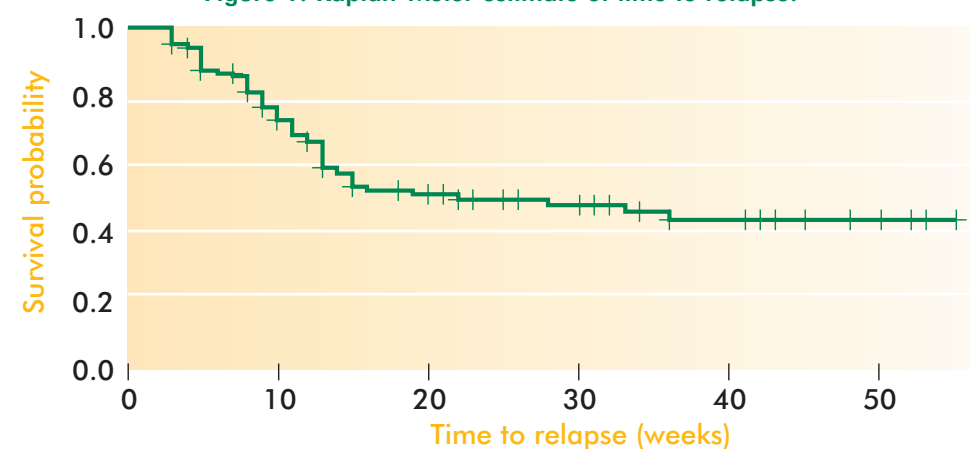


Figure 2: Kaplan–Meier estimate of time to relapse, by baseline Numeric Pain Rating Scale score.

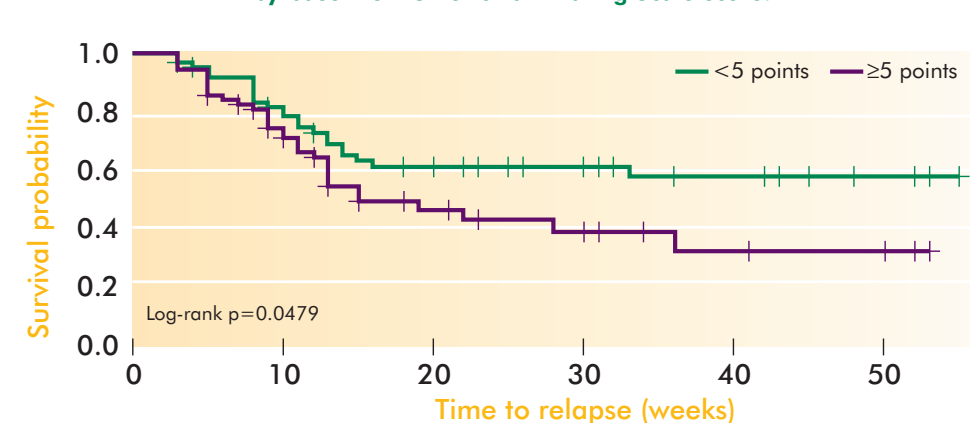
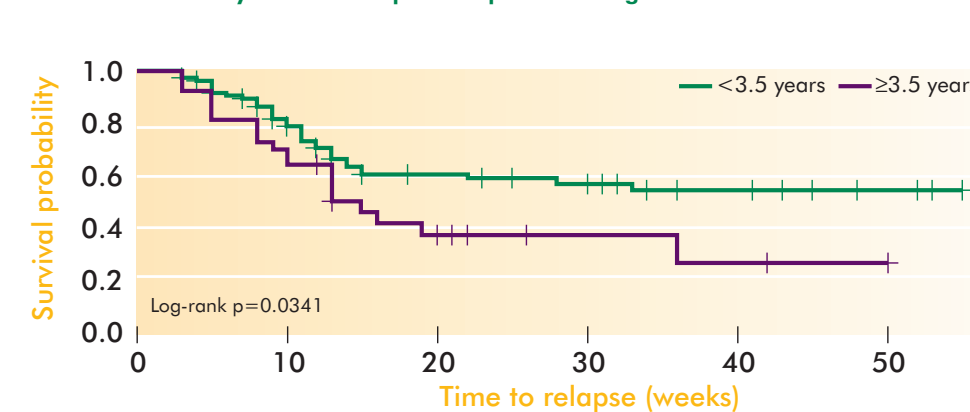
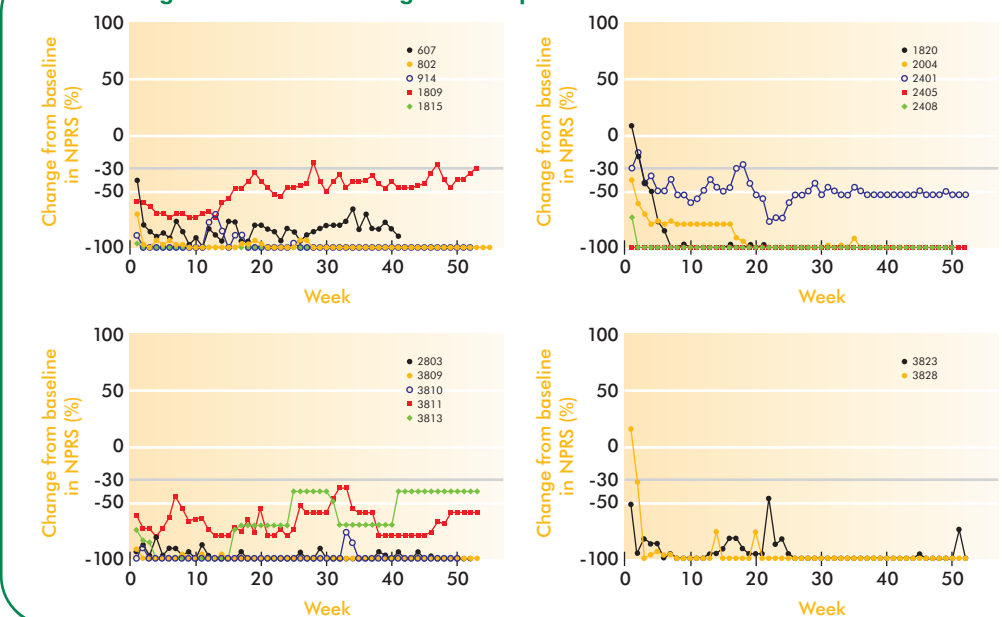


Figure 3: Kaplan–Meier time of weeks to relapse, by duration of post-herpetic neuralgia at baseline.



- The median duration of response was 22 weeks (Figure 1).
- Patients with lower baseline pain scores (NPRS score <5) and shorter PHN duration (<3.5 years) were more likely to have a longer duration of response (Figures 2 and 3, respectively).
- Duration of response to NGX-4010 was not correlated with any of the other parameters studied, that is, age, use of concomitant pain medication, the size of the treatment area, maximum pain increase on the treatment day or gender.
- Patients with greater pain reductions at Week 2 (≥40% reduction) also tended to have longer responses.
- Response to NGX-4010 was maintained for more than 40 weeks (long-term responders) in 17 patients (14%) (Figure 4).
- Ten (8%) patients became and remained pain-free for up to 52 weeks after a single NGX-4010 treatment (Figure 4).
- One patient who had had PHN for almost 22 years became and remained pain-free after a single NGX-4010 treatment at the end of the study (Week 52).

Figure 4: Profile of long-term responders to NGX-4010 treatment.



- Long-term responders to NGX-4010 treatment (patients who responded for more than 40 weeks) tended to be female, not taking concomitant neuropathic pain medications, had a slightly smaller treatment area, more pain increase on the day of treatment and lower baseline pain scores (Table 2).

Table 2: Baseline patient demographics and clinical characteristics (long-term responders to NGX-4010)

Characteristic	Long-term responders (n=17) [*]	Non-long-term responders (n=106)	Total (n=123)
Mean age, years – SD	67.4 – 15.4	69.9 – 9.8	69.6 – 10.7
Female, n (%)	12 (71)	56 (53)	68 (55)
Mean duration of PHN, years – SD [Range]	3.5 – 5.1 [0.5–21.7]	3.3 – 4.3 [0.3–32.3]	3.3 – 4.4 [0.3–32.3]
Mean baseline* average pain for the past 24 hours – SD	4.4 – 1.2	5.3 – 1.7	5.2 – 1.6
On concomitant pain medication [†] , n (%)	5 (29)	57 (54)	62 (50)
Mean size of painful area, cm ² – SD	258 – 213	352 – 231	339 – 231
Mean maximal increase in pain score on the treatment day – SD	3.1 – 3.2	1.8 – 3.0	2.0 – 3.0

PHN=post-herpetic neuralgia; SD=standard deviation.
^{*}Long-term responders were those patients who responded for more than 40 weeks.
^{*}Baseline pain level was defined as the mean of all available non-biased screening Numeric Pain Rating Scale scores in that category.
[†]A patient was defined as being on concomitant pain medication if pain medication started prior to the day of treatment, continued on the day of treatment, and was taken for at least 7 days.

CONCLUSIONS

- A single administration of the high-concentration capsaicin patch NGX-4010 can provide prolonged pain relief in patients with PHN.
- NGX-4010 is a promising new treatment option for patients with PHN.

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