NEUROGESX

NGX-4010, a High-Concentration Capsaicin Patch, in Painful Diabetic Neuropathy

LR Webster,[1] SK Gazda,[2] JR Medoff,[3] J Tobias,[4] GF Vanhove[4]

[1]Lifetree Clinical Research, Salt Lake City, Utah; [2]Integra Clinical Research, LLC, San Antonio, Texas; [3]Vital re:Search, Greensboro, North Carolina; [4]NeurogesX, Inc., San Mateo, California

BACKGROUND

- Painful diabetic neuropathy (PDN) is caused by damage to the sensory nerves, which may result from high circulating levels of glucose and glucose metabolites, and inadequate oxygenation of peripheral areas due to neurovascular damage
- Increased expression and function of the transient receptor potential vanilloid 1 (TRPV1) receptor appears to play a role in PDN[1,2]
  - Capsaicin is a potent agonist of the TRPV1 receptor that can defunctionalize TRPV1-expressing small-diameter sensory afferent fibers[3]
- NGX-4010, a high-concentration capsaicin dermal patch (capsaicin, 8%), significantly reduces neuropathic pain in patients with postherpetic neuralgia (PHN) or HIV-distal sensory polyneuropathy (HIV-DSP)[4-6]
- In the present study, the efficacy, safety, and tolerability of NGX-4010 was assessed in patients with PDN pretreated with 1 of 3 different topical anesthetics

METHODS

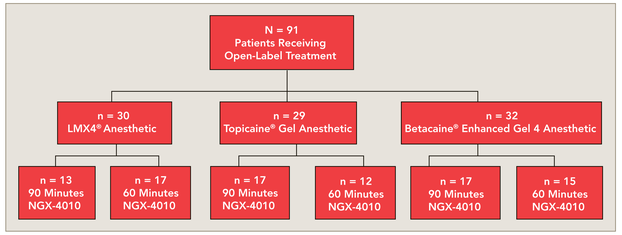
- This was a 12-week, open-label, randomized multicenter trial which included patients with moderate-to-severe PDN in both feet
  - For study inclusion, patients were required to have an average baseline Numeric Pain Rating Scale (NPRS) score of 3 to 8 inclusive, and have neuropathic pain in both feet for at least 3 months prior to the screening visit
  - Patients were excluded if they were currently using a topical pain medication (anti-inflammatory drugs, menthol, methyl salicylate, local anesthetics, steroids, or capsaicin) on the affected areas
- A single 60-minute pretreatment with 1 of 3 topical anesthetics (LMX4®, Topicaine®, or Betacaine®) was followed by a single 60- or 90-minute NGX-4010 application
- Primary efficacy variable
  - Percentage change in mean NPRS scores for "average pain for the past 24 hours" from Baseline during Weeks 2 to 12
- Secondary efficacy variables
  - Response rate
    - Proportion of patients achieving a ≥ 30% decrease in "average pain for the past 24 hours" NPRS score from Baseline during Weeks 2 to 12
    - Proportion of patients achieving a ≥ 50% decrease in "average pain for the past 24 hours" NPRS score from Baseline during Weeks 2 to 12
  - Overall improvement
    - Patient-rated Patient Global Impression of Change (PGIC) and investigator-rated Clinical Global Impression of Change (CGIC) scores at Weeks 2, 6, and 12
- Safety and tolerability measures
  - Continuous monitoring for adverse events (AEs); periodic assessments of clinical laboratory parameters, vital signs, and physical examination
  - Dermal assessments
  - Neurologic/sensory assessments
  - Rescue pain medication usage

RESULTS

Treatment Regimen

- 91 patients with PDN received treatment and were included in this analysis (**Figure 1**)
  - All 91 patients are included in the intent-to-treat (ITT) efficacy and safety populations

Figure 1. Patient flowchart.



Patient Demographics and Characteristics

- Patient characteristics were similar between the 60- and 90-minute treatment groups (**Table 1**)
  - Mean age of overall population was 58.7 years, 57% were male, most patients were white (76%), with a mean duration of pain of 5.0 years, and 51% of patients were receiving at least one concomitant neuropathic pain medication (anticonvulsants, non–selective serotonin reuptake inhibitor [non-SSRI] antidepressants, opioids)

Table 1. Patient Demographics and Characteristics.

	NGX-4010 90 Minutes	NGX-4010 60 Minutes	Total
No. of patients	47	44	91
Mean age, years (SD)	60.1 ± 11.08	57.3 ± 11.30	58.7 ± 11.21
Sex, % male	62	52	57
Race, n (%)			
Asian	1 (2)	0	1 (1)
Black or African American	7 (15)	3 (7)	10 (11)
White	33 (70)	36 (82)	69 (76)
Other	6 (13)	5 (11)	11 (12)
Mean weight, kg (SD)	92.0 ± 21.60	89.9 ± 19.75	100.7 ± 24.10
Mean duration of pain, years (SD)	4.8 ± 4.52	5.3 ± 4.87	5.0 ± 4.68
Mean pain level at screening (SD)	5.2 ± 2.32	5.0 ± 2.40	5.1 ± 2.35
"Average pain for the past 24 hours" at Baseline (mean ± SD)	5.6 ± 1.36	6.0 ± 1.46	5.8 ± 1.41
Number of subjects on concomitant neuropathic pain medication,* n (%)	22 (47)	24 (55)	46 (51)

*Anticonvulsants, non-SSRI antidepressants, opioids.

Effect of NGX-4010 Treatment on NPRS Scores

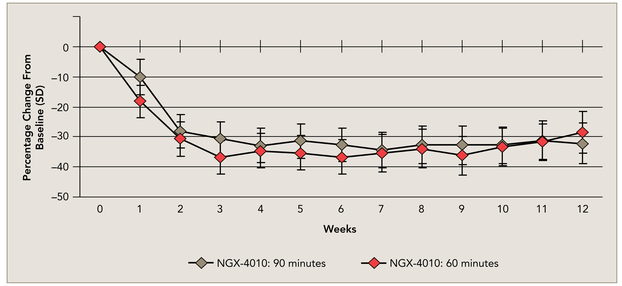
- After treatment with NGX-4010, the mean decrease from Baseline in NPRS scores was approximately 31% during Weeks 2 to 12 (**Table 2**)
- A decrease from Baseline in NPRS scores of ≥ 30% was observed in 47% of patients
  - 34% of patients had a ≥ 50% decrease from Baseline in NPRS scores (**Table 2**)

Table 2. Mean NPRS Scores for "Average Pain for the Past 24 Hours" (ITT Population).

	NGX-4010 90 Minutes	NGX-4010 60 Minutes	Total
Baseline (SD)	5.6 (1.4)	6.0 (1.5)	5.8 (1.4)
Weeks 2 to 12			
Change from Baseline (SD)	−1.6 (2.1)	−1.9 (2.2)	−1.8 (2.2)
Percentage change from Baseline (SD)	−30.7 (37.4)	−32.2 (34.8)	−31.4 (36.0)
Patients with ≥ 30% decrease from Baseline during Weeks 2 to 12, n (%)	22 (47)	21 (48)	43 (47)
Patients with ≥ 50% decrease from Baseline during Weeks 2 to 12, n (%)	15 (32)	16 (36)	31 (34)

- NPRS scores improved during the first 2 weeks of treatment, and then were maintained over the remainder of the 12-week study period (**Figure 2**)
  - The improvements were similar for the 60- and 90-minute applications

Figure 2. Mean NPRS scores for Weeks 1 to 12 after NGX-4010 application.



Effect of NGX-4010 Treatment on Overall Improvement

- Improvements in PGIC were observed as early as Week 2 (**Table 3**)
  - 48% of patients reported being much/very much improved at Week 2
- PGIC improvements continued through Week 12
  - 45% of patients reported being much/very much improved at Week 6
  - 37% of patients reported being much/very much improved at Week 12

Table 3. Patient Global Impression of Change.

Patient Global Impression of Change (PGIC)	
Improved (very much, much), n (%)	
Week 2	42/88 (48)
Week 6	40/89 (45)
Week 12	32/86 (37)

Safety

- Application site reactions, including burning and pain, were the most common treatment-related adverse events (**Table 4**)
  - AEs were generally mild or moderate in severity

Table 4. Treatment-Related Adverse Events Occurring in > 1% of Subjects in the Total NGX-4010 Group.

	NGX-4010 90 Minutes	NGX-4010 60 Minutes	NGX-4010 Total
Application site events, n (%)			
Burning	8 (17)	7 (16)	15 (16)
Dermatitis	1 (2)	1 (2)	2 (2)
Dryness	1 (2)	2 (5)	3 (3)
Pain	5 (11)	2 (5)	7 (8)
Pruritis	3 (6)	1 (2)	4 (4)
Swelling	2 (4)	3 (7)	5 (5)
Blood pressure increased, n (%)	1 (2)	1 (2)	2 (2)

- Neurologic evaluations demonstrated that the majority of subjects had either no change or an improvement in neurologic function following treatment (**Table 5**)

Table 5. Neurologic Evaluations at Screening and 12 Weeks After NGX-4010 Application.

	Screening	Week 12	Change From Screening to Week 12	
Deep Tendon Reflex				
n	85	85	n	85
Absent	57 (67%)	57 (67%)	Decreased	7 (8%)
Diminished	19 (22%)	19 (22%)	No Change	69 (81%)
Normal	8 (9%)	9 (11%)	Increased	9 (11%)
More Brisk Than Normal	1 (1%)	0	Increased Above Normal	0
Very Intense	0	0		
Vibration				
n	85	85	n	85
Absent	22 (26%)	19 (22%)	Decreased	10 (12%)
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Normal	30 (35%)	43 (51%)	Increased	12 (14%)
Increased	6 (7%)	6 (7%)	Increased Above Normal	1 (1%)

SUMMARY

- A single 60- or 90-minute treatment with NGX-4010 reduced pain over a 12-week period in patients with PDN
- NGX-4010 treatment resulted in a mean 31% decrease in NPRS scores from Baseline during Weeks 2 to 12, and 47% of patients had a clinically meaningful response (≥ 30% decrease in NPRS score from Baseline)
- Treatment with NGX-4010 appeared to be generally safe and well tolerated
- Treatment-related AEs were typically transient and application site specific, occurring on the day of treatment or shortly thereafter
  - Application site AEs were generally similar for the 2 treatment durations
- No evidence suggesting impairment of neurologic function was observed following treatment

CONCLUSION

- The high-concentration capsaicin NGX-4010 patch, in conjunction with any of the 3 topical local anesthetics tested, was generally safe and reduced pain over a 12-week period in patients with PDN

REFERENCES

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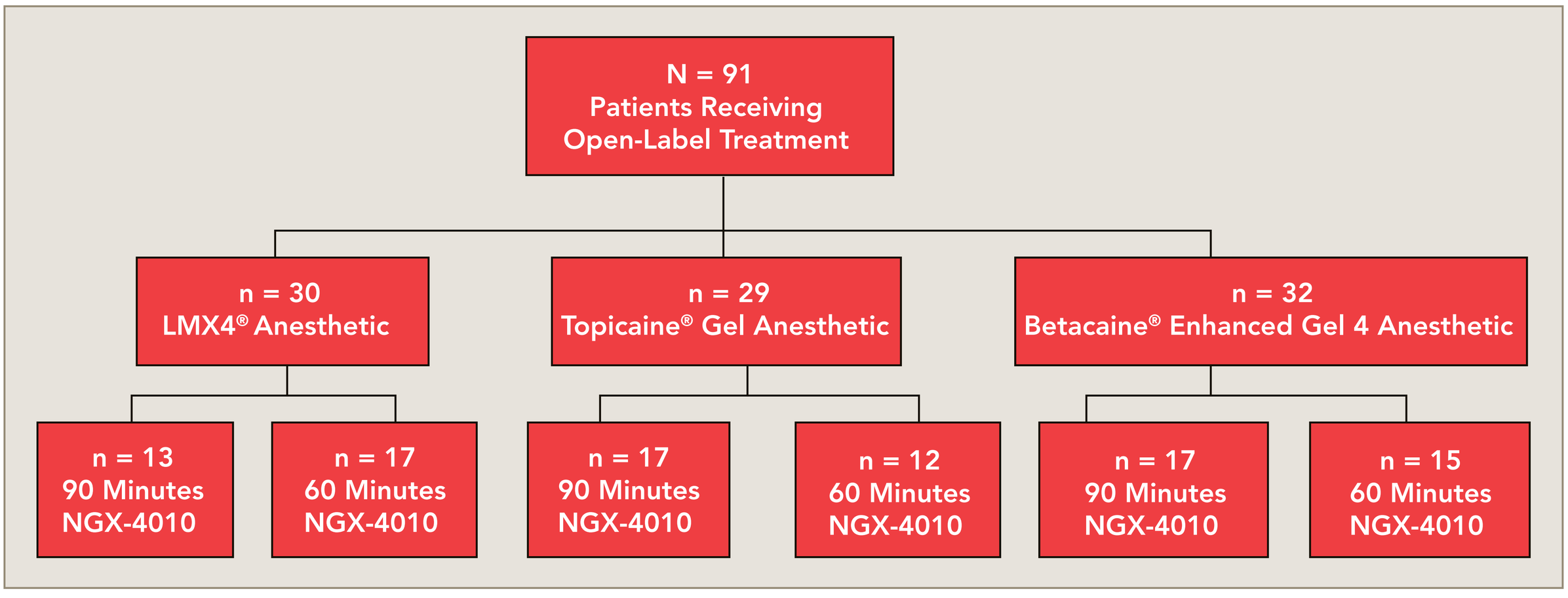

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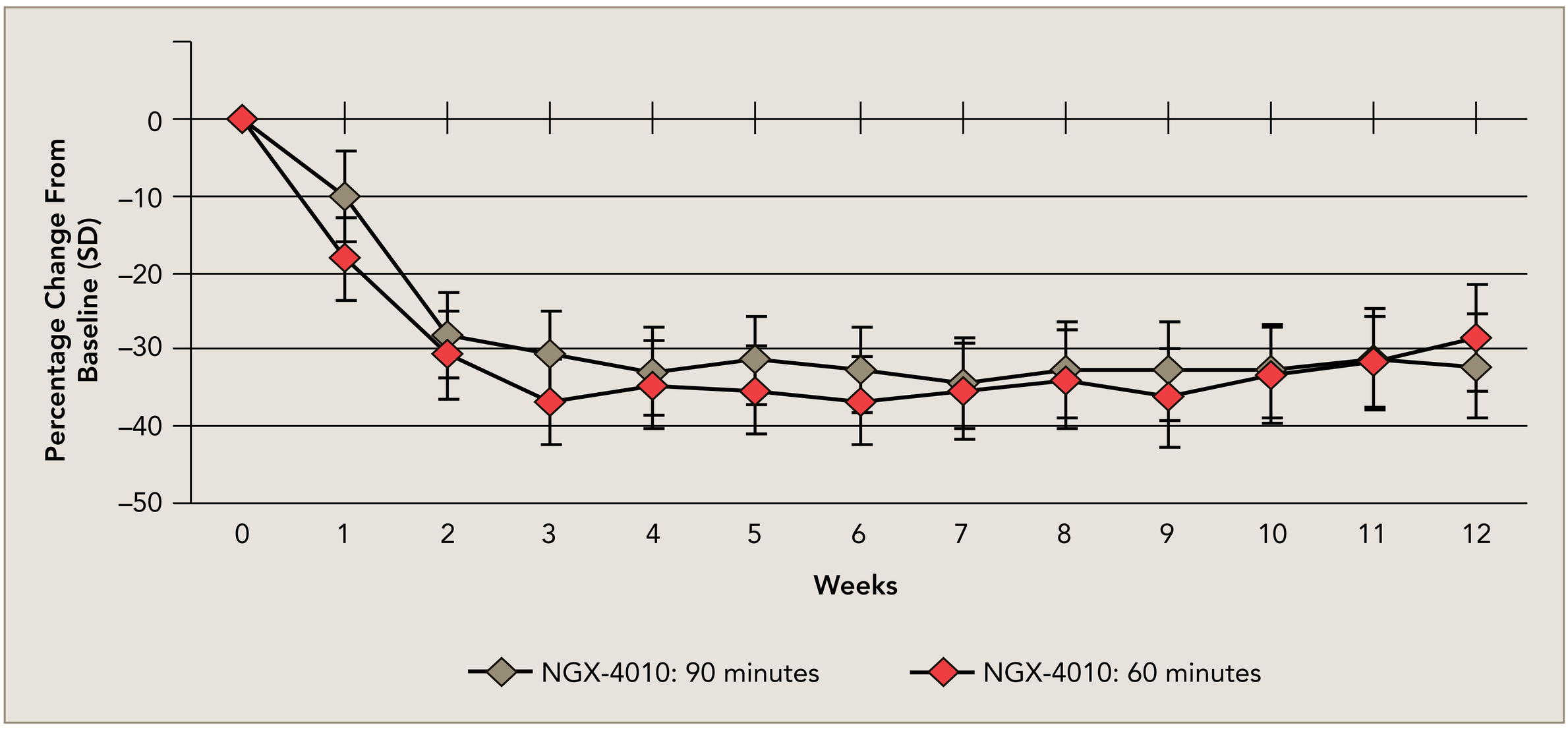

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