Pain Severity in CRPS-1 Relative to Other Painful Conditions: Meta-Analysis and Mapping of Neridronate Treatment Response

Brian Cuffel, PhD[1]; Stephen Bruehl, PhD[2]; Karina Gritsenko, MD[3]; Gail Cawkwell, MD, PhD[1]
[1]Ambros Therapeutics, Inc.; [2][Bruehl institution]; [3][Gritsenko institution] Corresponding Author Brian Cuffel bcuffel@ambrostx.com

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Background

- Complex Regional Pain Syndrome-Type I (CRPS-1) is a severe chronic pain condition with substantial disability and reduced quality of life[1]
- Neridronate is under development in the US for CRPS-1 with warm symptoms and positive triple phase bone scan.
- A prior clinical trial demonstrated reductions in Short-Form McGill Pain Questionnaire (SF-MPQ) scores in neridronate-treated CRPS-1 patients versus placebo at Day 40[2] but the clinical importance of average treatment effects is difficult to interpret

Objective

- Characterize CRPS-1 pain severity relative to other chronic pain conditions using the SF-MPQ and map the neridronate treatment response from the NERIAS trial onto the resulting reference distribution

Methods

- Systematic literature review searched PubMed (2/23/2026) for studies reporting SF-MPQ scores across painful conditions
- Eligibility: original 15-item SF-MPQ3, trial N≥40, mean age and sex reported, well-defined pain condition, no minimum pain entry requirement

Methods (continued)

- Of 256 articles identified, 13 studies across 8 conditions met the inclusion criteria
- The pooled reference pain distribution was estimated using random-effects meta-regression
- SF-MPQ severity bands were defined as pooled mean ±1 SD.
- CRPS severity was estimated from a prospective RSDSA observational cohort (N=501 with analyzable SF-MPQ data) by Ambros Therapeutics. The cohort included CRPS Type 1 and 2.
- Neridronate treatment response from NERIAS (NERI-AS001-07; Abiogen Pharma S.p.A.), which enrolled patients with moderate-to-severe CRPS-1 (baseline VAS pain ≥50 mm)
- All analyses were conducted in R (version 4.5.2) using the *meta* package for random-effects meta-regression

Results

- The pooled non-CRPS SF-MPQ reference distribution had a mean of 12.7 (95% CI: 10.1-15.6, SD 8.9) (Table 1). The lower severity band is <3.8, the moderate band is 3.8–21.7, and the higher severity band is >21.7
- The RSDSA cohort had a mean SF-MPQ of 28.1 (SD 9.4), confirming higher pain severity in this real-world CRPS sample (Figure 1)
- Neridronate-treated CRPS-1 participants in the NERIAS study's baseline mean SF-MPQ of 22.68 was in the higher severity band and ranked at the 87th percentile of the reference distribution, exceeding chronic pelvic pain (18.9), rheumatoid arthritis (17.3), chronic low back pain (14.1), and post-surgical conditions (2.4–14.2)

Results (continued)

- Following neridronate treatment in NERIAS, SF-MPQ scores declined to the 31st percentile (8.3) at Day 40 - a reduction of 14.4 points and 55 percentile points (Figure 2)
- Placebo change in NERIAS was 4.2 points; placebo-adjusted treatment difference was 10.2 points, representing a drug-attributable shift of 38 percentile points

Conclusions

- CRPS-1 ranks among the highest pain intensity burdens across 8 chronic pain conditions as measured by a reference distribution of SF-MPQ scores and confirmed by a large prospective CRPS cohort
- Neridronate treatment produced a meaningful reduction in pain severity, shifting the average patient from the higher to the moderate severity band
- Mapping the NERIAS trial of neridronate therapy results onto the reference distribution translates average treatment effects into a concrete percentile shift that communicates clinical significance to payers, clinicians, and patients

Limitations

- A limited set of chronic pain conditions were identified in the literature and cross-study comparisons are subject to bias. Concomitant and background therapies in the included studies were not characterized and may have influenced the observed pain severity.

Table 1. Included studies: SF-MPQ pain intensity by condition

Citation	N	Mean Age	Female (%)	SF-MPQ Mean
Berry (2006)	635	70.5	0.0	6.2
Beattie (2004)	373	48.3	53.0	16.5
Marin (2006)	266	47.0	43.0	15.0
Sezgin (2015)	100	50.2	50.0	16.7
Martí-Salvador (2018)	66	42.6	56.1	17.8
Das (2024)	60	42.2	41.6	11.7
Muduli (2025)	60	40.2	66.7	7.3
Droz (2011)	331	34.0	100.0	18.9
Prakash (2023)	49	46.5	59.2	9.9
Truong (2005)	59	63.0	100.0	2.4
Tzikos (2025)	99	63.7	18.5	14.2
Wang (2019)	40	55.8	33.3	13.3
Blake (2006)	58	62.8	79.1	17.3

Bone mets advanced prostate cancer | Chronic Low Back Pain | Chronic Pelvic Pain | Lumbar Spondylosis | PostSurgical Breast | PostSurgical GIST | Primary Trigeminal Neuralgia | Rheumatoid Arthritis

Figure 1. Pain intensity in CRPS compared to other pain conditions

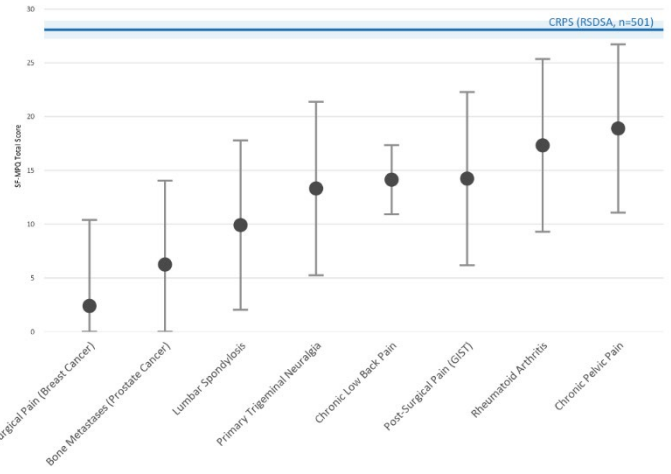
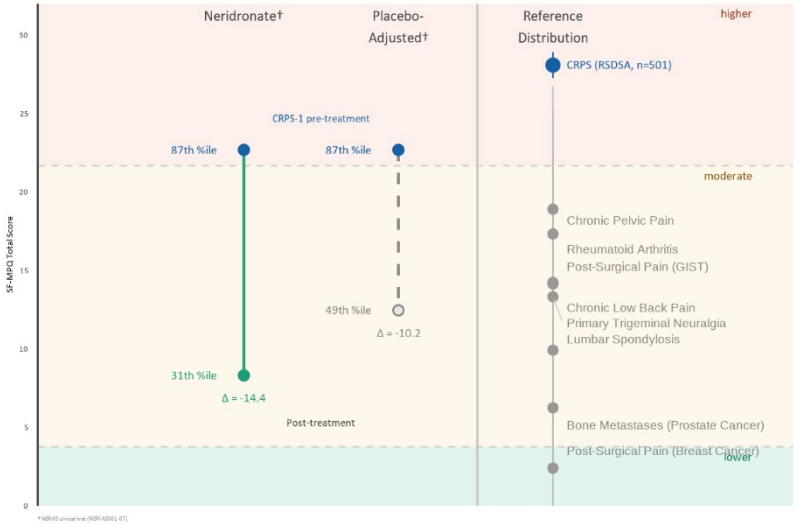


Figure 2. Pain intensity across chronic pain conditions and neridronate treatment response



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Disclosures
K. Gritsenko: advisory board member for Pacira, Vertex, Scilex and consultant for Ambrose, Pacira, and Vertex. B Cuffel & G Cawkwell: employees of Ambros; S Bruehl: consultant for Ambros and Akigai.

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