Clinical Trials Cover Page: Study Protocol and Statistical Analysis Plan

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Multimodal Treatment for Hemiplegic Shoulder Pain

NCT02893267

Expectations and Analysis

Compare the efficacy of PNS vs. PT in reducing HSP.

Hypothesis 1. The reduction in HSP will be greater in PNS alone vs. PT alone. Based on Preliminary Studies 1 and 2, an average reduction of 5 points (63%, assuming baseline of 8) in BPI SF-3 is anticipated for the PNS+shamPT group by EOT with maintenance of this effect at follow-up (Figure 7). Based on Preliminary Study 2, a 34% reduction is anticipated by the end of treatment for PT+shamPNS group, increasing to a 20% decrease by the end of follow-up. We anticipate an 87.5% reduction, or 2-points more than PT +shamPNS, by end of treatment for the PNS+PT group, maintaining this level at the end of follow up. The anticipated difference of at least 2.0 points between groups at 28-wks is the minimum clinically important difference in pain scores.152 153 In order to detect this difference with 80% power, α=0.05 (combined), and anticipated SD of 2.4, the minimum sample size is 27/group is necessary when using a one-sided, two-sample, equal-variance t-test of 3 pairwise comparisons (assuming pain reduction with PNS + PT > PNS+shamPT > PT + shamPNS). With the anticipated drop-out rate of 20%, this leads to a sample size of 32/group for a total of 96 participants.

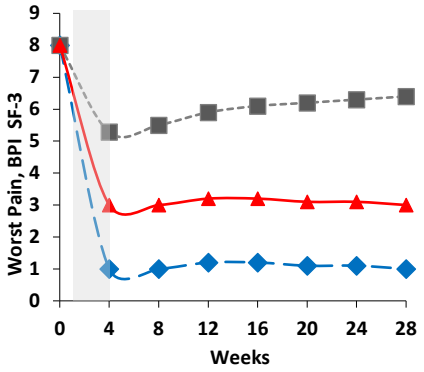

Figure 7: Anticipated average BPI SF-3 trajectories for participants assigned to PNS+PT (dashed, diamond) PNS+shamPT(solid, triangle), and PT+shamPNS (dotted, square). Shaded area indicates treatment.

Exploratory looks at the data across the three groups are done first before fitting our models. Poolability of data across sites will be evaluated and adjusted for as needed. Comparability of demographics by site will be assessed. Treatment by site interaction will be tested. Each measure will be modeled using a linear mixed effects approach which is well-suited for handling correlated repeated measurements, unbalanced data, missing data and dropouts in longitudinal studies. These mixed effects models yield estimates of the treatment, time and treatment by time while permitting us to control for potential confounders. Analysis for comparison of responders will be completed with logistic regression analysis with treatment group as independent variable.

AIM 2. Compare the efficacy of PNS + PT, PNS + ShamPT, and PT + ShamPNS in reducing HSP.

Hypothesis 2. The reduction in HSP will be the greatest with PNS + PT, followed by PNS + Sham PT, and finally PT + Sham PNS. Continuous data will be analyzed using the approach described for hypotheses 1. As a phase II trial, power analysis was conducted only for the primary outcome measure (Worst Pain in the Last Week, BPI SF-3).