INTRODUCTION

A spontaneous nociceptor-based mechanism is thought to underlie OA pathology, involving an imbalance between nociceptive input and pain inhibition. This imbalance can result in chronic pain, disability, and reduced quality of life for patients with OA. CNTX-4975 is a recombinant human calcitonin gene-related peptide (rhCGRP) that has demonstrated analgesic properties in preclinical models and clinical trials for OA. This randomized, double-blind, placebo-controlled trial assessed the efficacy and safety of CNTX-4975 administered as a single intramuscular injection in subjects with knee OA.

METHODS

Study Design

This was a prospective, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of CNTX-4975 administered as a single intramuscular injection in subjects with knee OA. Subjects were randomized to receive CNTX-4975 0.5 mg (n=34), CNTX-4975 1.0 mg (n=71), or placebo (n=34) in the index knee. The primary end point was the change from baseline to week 12 in the weekly average WOMAC A1 pain score. Secondary end points included change from baseline to week 12 in the LS mean change from baseline in WOMAC A1 pain score, LS mean change from baseline in PSFS score, LS mean change from baseline in AUC of daily WOMAC A1 pain scores, and percentage of subjects who achieved ≥50% improvement in WOMAC A1 pain score.

RESULTS

Subjects

A total of 141 subjects were randomized to receive CNTX-4975 0.5 mg (n=34), CNTX-4975 1.0 mg (n=71), or placebo (n=34) in the index knee. Baseline characteristics were similar across the treatment groups. The most commonly reported TEAEs (incidence >5%) were arthralgia (8.8%), upper respiratory tract infection (5.9%), OA (5.9%), and joint effusion (8.8%).

Safety: All subjects who received any amount of CNTX-4975 or placebo were included in the safety population. The most frequently reported TEAEs were reported by 30% (placebo), 47% (CNTX-4975 0.5 mg), and 48% (CNTX-4975 1.0 mg). The most common TEAEs were arthralgia (8.8%), upper respiratory tract infection (5.9%), OA (5.9%), and joint effusion (8.8%).

Efficacy

When adjusting for use of rescue medications, a statistically significant reduction in weekly average WOMAC A1 pain scores at week 12 for placebo versus CNTX-4975 0.5 mg and CNTX-4975 1.0 mg in the per-protocol population was observed (LSMD: -2.5 [95% CI: -4.7, -0.3], P<0.01, CNTX-4975 versus placebo.

CONCLUSIONS

CNTX-4975 1.0 mg provided statistically significant improvements in pain intensity and health status at week 12. Subjects treated with CNTX-4975 1.0 mg for the use of rescue medications had a statistically significant improvement in functional outcomes based on a validated scoring system in 70% of subjects. Further studies are needed to determine the long-term effects of CNTX-4975 on pain and function in subjects with knee OA.