



## ORAL CALCITONIN DEMONSTRATED SYMPTOM-MODIFYING EFFICACY AND INCREASED CARTILAGE VOLUME: RESULTS FROM A 2-YEAR PHASE 3 TRIAL IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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### *Abstract:*

**Purpose:** To evaluate the symptom- and structure-modifying efficacy and safety of oral salmon calcitonin (oCT) formulated with a 5-CNAC carrier (a molecule based on Eligen<sup>®</sup> technology from Emisphere), in patients with moderate to severe knee pain and structural damages classified as Kellgren-Lawrence 2-3 due to osteoarthritis (OA).

**Methods:** A total of 1169 men and women aged 50-80 years with a mean BMI of 28.9 kg/m<sup>2</sup> who had painful OA of the knee with structural manifestations were enrolled in this multi-center, double-blind, randomized placebo-controlled study. Patients received (1:1) oCT 0.8 mg twice daily or placebo for 24 months; rescue medication was allowed in both arms. The primary efficacy endpoints were joint-space width (JSW), WOMAC pain and function visual analogue scale scores after 24 months in the signal knee. Secondary endpoints included but were not limited to WOMAC stiffness, patient and physician global assessments, and knee cartilage degradation. Safety endpoints were adverse events (AEs) and tolerability.

**Results:** Baseline values were well matched between the two groups. In ITT analysis at 24 months, oCT treatment did not have an effect on JSW ( $p=0.97$ ; progression was -0.2 mm in both groups). However, oCT increased cartilage volume by a mean 4.8% (0.73%) [vs 2.5% (0.61%) in placebo group,  $p=0.012$ ]. Furthermore, oCT resulted in significant changes (vs placebo) in WOMAC pain [-115.7 (4.9) vs -94.9 (4.8) mm;  $p=0.002$ ], function [-338.7 (16.7) vs -283.0 (15.8) mm;  $p=0.013$ ] (see Figure) and stiffness [-44.1 (2.2) vs -32.6 (2.1) mm;  $p<0.001$ ] scores (numbers in parentheses are standard errors). Improvement was also obtained in the oCT group (vs placebo) in VAS 24 hour pain ( $p=0.018$ ), patient global assessment ( $p=0.008$ ) and physician global assessment ( $p=0.014$ ). The discontinuation rate was 33% for oCT vs 23% for placebo treatment. Drug-related AE discontinuations occurred in 19.5% oCT group (vs 5.8% in placebo group), mostly happening early in the oCT group then parallel to placebo. The most common AEs in the oCT group (vs placebo) were hot flush (17.8 vs 4.1%), nausea (14 vs 3.1%), dyspepsia (10.1 vs 4.5%) and diarrhoea (9.6 vs 4.3%), and accounted for most discontinuations. Immunogenicity was noted in 17.4% (oCT) vs 1.6% (placebo) at 24 months.

**Conclusions:** Twice daily oCT over 2 years resulted in a significant symptom-modifying efficacy in patients with painful knee OA as assessed by WOMAC pain, physical function, and stiffness scores. Although improvement on the primary endpoint of JSW was not reached, there was an increase in cartilage volume vs placebo indicating some structure-modifying efficacy. Safety and tolerability of oCT was largely in line with previous clinical experience with calcitonins.

Figure: Select efficacy variables: mean changes over two years

