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## **Radiographic Outcomes Were Concordant with Pain and Function Response: Post-Hoc Analysis from a Phase 2 Study of SM04690, a Wnt Pathway Inhibitor for Knee Osteoarthritis Treatment**

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**Purpose:** SM04690, a Wnt pathway inhibitor, is a potential disease modifying knee osteoarthritis (KOA) drug. A phase 2 study evaluated Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscore and medial joint space width (mJSW) changes. To test the hypothesis that mJSW changes are associated with WOMAC subscore improvements, post-hoc concordance analyses were performed.

**Methods and Materials:** KOA subjects, Kellgren-Lawrence (KL) grades 2-3, received 2 mL intra-articular SM04690 (0.03, 0.07, 0.23 mg) or placebo (PBO) in target knees. WOMAC Pain [0-50], Function [0-170], and mJSW were assessed over 52 weeks. Logistic regression analyses generating receiver-operator characteristic (ROC) curves estimated concordance between mJSW change and subjects who achieved WOMAC Pain and Function improvements  $\geq 50\%$  and  $\geq 20$  [of 100] points response. ROC area under curve (AUC)  $> 0.7$  was 'acceptable' and  $> 0.8$  'excellent'.<sup>1</sup> ITT as observed and two subgroups were analyzed: 1) unilateral symptomatic (pre-specified: UNI) and 2) UNI without widespread pain or comorbid symptoms (Widespread Pain Index  $\leq 4$  and Symptom Severity  $\leq 2$ , post-hoc: UNI-WP).

**Results:** 455 subjects were enrolled (age 60.3 years, BMI 29.9 kg/m<sup>2</sup>, 268 [58.9%] female, 292 [64.2%] KL 3, 164 [36.0%] UNI KOA).

At Week 52, response was achieved in ITT (53%), UNI (56% [0.03 mg], 63% [0.07 mg], 64% [0.23 mg], 47% [PBO]), and UNI-WP (56% [0.03 mg], 62% [0.07 mg], 70% [0.23 mg], 44% [PBO]). 0.03 mg (UNI, NS; UNI-WP, P=0.047) and 0.07 mg (UNI, P=0.009; UNI-WP, P=0.013) doses also demonstrated increased mJSW compared to PBO.

In ITT, no group achieved acceptable concordance (Figure); in UNI only 0.07 mg dose achieved acceptable concordance (AUC=0.783), and UNI-WP 0.07 mg dose achieved excellent concordance (AUC=0.825).

**Conclusion:** In UNI and UNI-WP KOA subjects treated with SM04690 0.07 mg in this study, concordance was demonstrated between structure (mJSW change) and clinical outcomes (WOMAC Pain and Function response).

<sup>1</sup>Hosmer DW & Lemeshow S. (2000). Applied Logistic Regression.

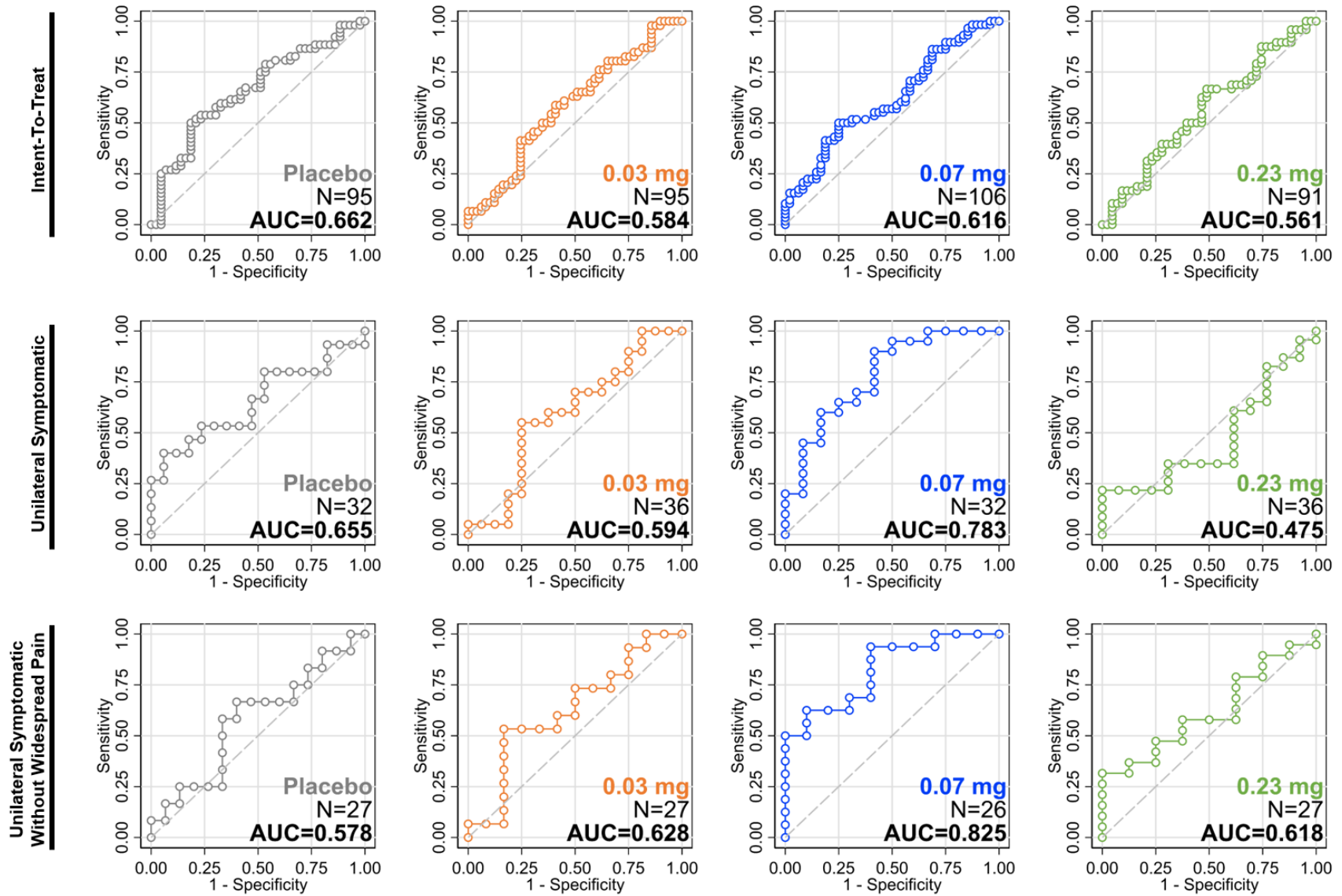


Figure. ROC Curves Illustrating Concordance between WOMAC Pain and Function Response and mJSW Change by Treatment Group and Analysis Group