Accepted as poster #P41 at the 6th World Congress on Controversies, Debates & Consensus in Bone, Muscle & Joint Diseases (BMJD), Bangkok, Thailand, November 8-10, 2018

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

Jeyanesh R. S. Tambiah[1], Christopher Swearingen[1], Sarah Kennedy[1], and Marc Hochberg[2]

[1]Samumed, LLC, San Diego, CA
[2]University of Maryland School of Medicine, Baltimore, MD

Problem statement: 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: 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 the target (most painful) knee. 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 ≥50% and ≥20 [of 100] points response. ROC area under curve (AUC) > 0.7 was 'acceptable' and > 0.8 'excellent. Intent-to-treat (ITT) and two subgroups were analyzed: 1) unilateral symptomatic (pre-specified: UNI) and 2) UNI without widespread pain or comorbid symptoms (Widespread Pain Index ≤4 and Symptom Severity ≤2, post-hoc: UNI-WP).

Results: 455 subjects were enrolled (age 60.3 years, BMI 29.9 kg/m^2, 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 with PBO.

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

Disclosures of interest: J. Tambiah, C. Swearingen, and S. Kennedy are shareholders and employees of Samumed, LLC; M. Hochberg: consultant for Bioberica, EMD Serono, Novartis Pharma AG, Plexxikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, and Theralogix, LLC.

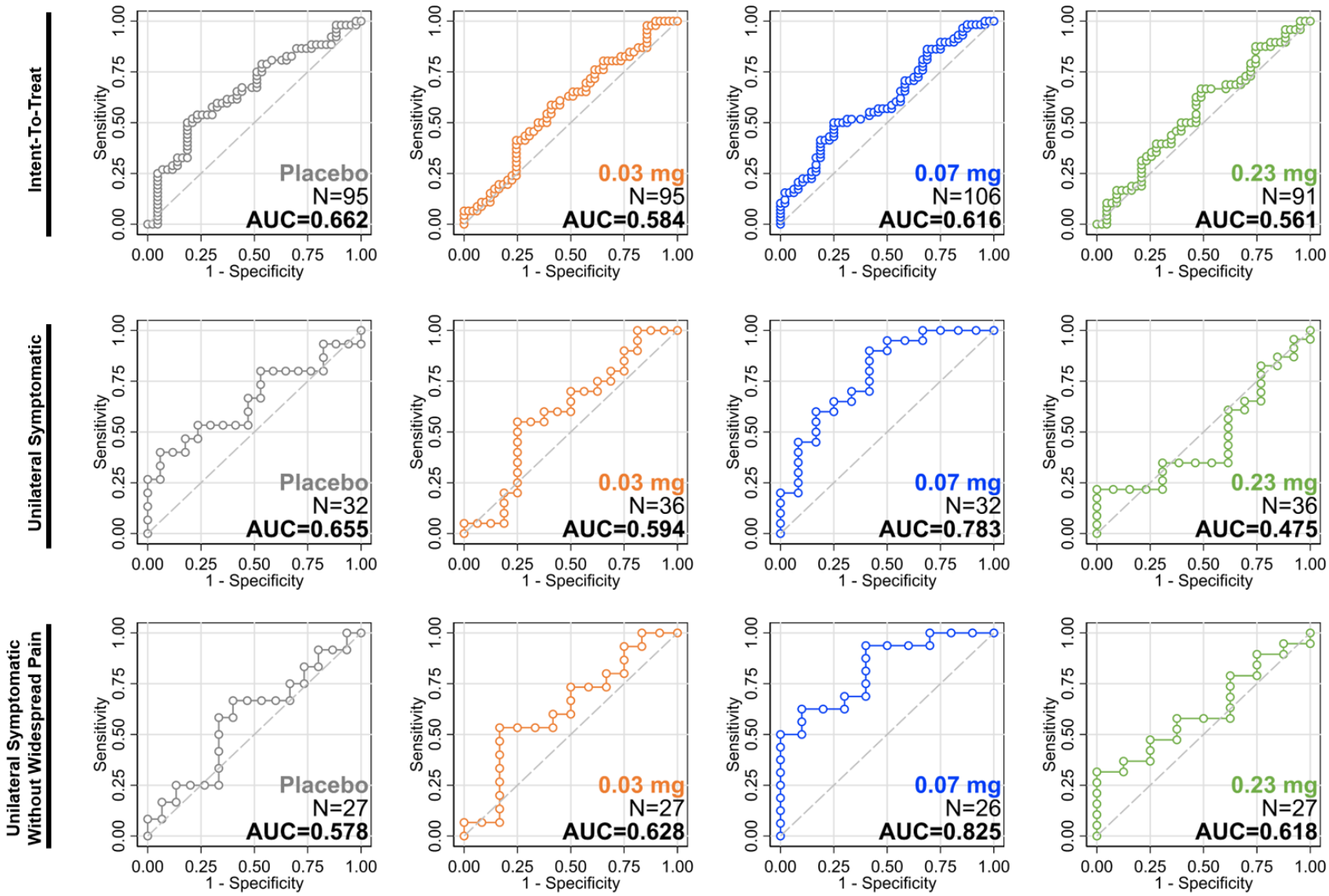

Figure. ROC Curves Illustrating Concordance between WOMAC Pain and Function Response and mJSW Change by Treatment Group and Analysis Group