

FRI0534

RADIOGRAPHIC OUTCOMES WERE ASSOCIATED WITH PAIN AND FUNCTION RESPONSES: POST-HOC ANALYSIS FROM A PHASE 2 STUDY OF A WNT PATHWAY INHIBITOR, SM04690, FOR KNEE OSTEOARTHRITIS TREATMENT

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Background: SM04690, a small molecule intra-articular (IA) Wnt pathway inhibitor is in development as a potential disease modifying knee osteoarthritis drug. A phase 2, 52 week, randomised controlled trial evaluated changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain and Function and medial joint space width (mJSW). It was hypothesised that observed mJSW increases led to WOMAC subscore responder improvements. To address this question, a concordance analysis was performed.

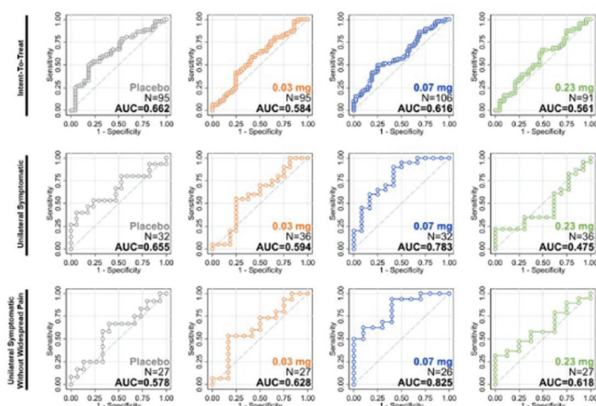
Objectives: To evaluate concordance, or level of agreement, between mJSW and WOMAC Pain and Function 'responders.'

Methods: Subjects with ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received 2 mL IA SM04690 (0.03, 0.07, or 0.23 mg) or placebo (PBO) in the target (most painful) knee. WOMAC Pain [0–50] and Function [0–170] were assessed at Weeks 0, 4, 13, 26, 39 and 52 and knee radiographs at Weeks 0, 26 and 52. Baseline-adjusted logistic regression group analyses estimated concordance between mJSW change and pain and function changes for responders who achieved both WOMAC Pain and Function improvements of >50% and >20 [scaled to 100] points. Receiver-operator characteristic (ROC) curves were generated with area under curve (AUC) to estimate concordance (AUC >0.7='acceptable' and >0.8='excellent' concordance¹). ITT and two subgroups were analysed: 1) unilateral symptomatic knee OA (pre-specified: UNI) and 2) unilateral symptomatic knee OA without widespread pain or comorbid symptoms (Widespread Pain Index ≤4 and Symptom Severity ≤2, post-hoc: UNI-WP).

Results: 455 subjects were enrolled (mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m², 268 [58.9%] female, 292 [64.2%] KL Grade 3, 164 [36.0%] UNI knee OA).

In the ITT, approximately 53% were responders across all groups. In UNI, 20 (56%) 0.03 mg; 20 (63%) 0.07 mg; 23 (64%) 0.23 mg and 15 (47%) PBO, and in UNI-WP, 15 (56%) 0.03 mg; 16 (62%) 0.07 mg; 19 (70%) 0.23 mg and 12 (44%) PBO were responders. The 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 at Week 52.

In ITT, no treatment group achieved AUC >0.7 (figure 1). In UNI, the 0.07 mg dose demonstrated 'acceptable' concordance between response and mJSW (AUC=0.783). In UNI-WP, the 0.07 mg dose showed 'excellent' concordance (AUC=0.825).



Abstract FRI0534 – Figure 1. ROC Curves Illustrating Concordance between WOMAC Pain and Function Response and mJSW Change by Treatment Group and Analysis Group

Conclusions: In this post-hoc analysis, treatment with SM04690 maintained or increased mJSW in the 0.03 and 0.07 mg doses compared to PBO over 52 weeks. In UNI and UNI-WP 0.07 mg cohorts, changes in mJSW were concordant with WOMAC Pain and Function response.

REFERENCE:

- [1] Hosmer DW, Lemeshow S. Applied Logistic Regression 2000. New York: John-Wiley & Sons, Inc.

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FRI0535

THE CLINICAL AND RADIOGRAPHIC EARLY COURSE OF KNEE AND HIP OSTEOARTHRITIS OVER 10 YEARS IN CHECK (COHORT HIP AND COHORT KNEE)

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Background: Osteoarthritis (OA) is the most prevalent joint disease and one of the leading causes of chronic pain and disability worldwide. Yet, relatively little is known about the early course of OA.

Objectives: To describe the clinical and radiological early course of hip and/or knee OA.

Methods: CHECK (Cohort Hip and Cohort Knee) is a multicenter, prospective observational cohort study of 1002 participants. Inclusion criteria were: 1) age 45–65 years at the time of inclusion, 2) pain in knee(s) and/or hip(s), 3) never or not longer than 6 months ago for the first time consulted a physician for these symptoms. Participants were included through general practitioners and advertisements. Visits took place at baseline, and at 2, 5, 8, and 10 year follow-up (T0, T2, T5, T8 and T10). At each visit, questionnaires, including joint pain presence (Numeric rating score, NRS), morning stiffness, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), were inquired, and physical examination, and x-ray imaging were performed. Clinical OA was defined by the clinical American College of Rheumatism (ACR) criteria. Radiographic OA (ROA) was defined as Kellgren and Lawrence score (K and L) of ≥2.

Results: 1002 participants (age 56±5 years (mean ±sd); 79% female; BMI 26±4 kg/m²) were included. 83% reported knee pain at baseline, 59% reported hip pain, and 42% reported both. 10 year follow-up data were complete for 85% of the participants. The total WOMAC score showed a median of 21 (range 0–80) at baseline and remained rather constant over time (T2=20 (0–83); T5=20 (0–86); T8=19 (0–88); T10=19 (0–81)). The same was observed for pain (NRS). At baseline, 520 participants fulfilled the clinical ACR criteria for knee and/or hip OA. Of these, only 91 (17.5%) participants subsequently fulfilled the ACR criteria at every follow-up visit. 138 participants did never fulfil the clinical ACR criteria for hip or knee OA. At baseline, 157 participants showed ROA in on or both knees and 161 participants showed ROA in on or both hips. After 10 years follow-up, 601 (60%) participants had ROA in one or both knees and 513 (51%) participants had hip ROA in one or both hips. Of those with hip OA in at least one hip, 256 (50%) had bilateral knee ROA at T10. Of the participants with knee OA in at least one knee, 256 (43%) had bilateral hip ROA at T10. Most joint replacements took place between 2 and 8 years follow-up (11 knees, 29 hips), predominantly in participants with multiple affected joints. Only 115 (13.5%) participants did not develop ROA of knee or hip.

Conclusions: Although mean pain scores remain fairly stable over time, individual scores tend to fluctuate over time. Therefore, only few participants constantly fulfil the clinical criteria for OA. More than half of the participants had ROA after 10 year follow-up and a large overlap of knee and hip ROA was observed. Numbers of joint replacements were highest in participants developing both hip and knee OA.

Disclosure of Interest: None declared

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FRI0536

PREGABALIN EFFICACY IN TREATMENT OF CHRONIC PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Modern methods of treatment of osteoarthritis have mainly anti-inflammatory action. A few studies show the effectiveness of centrally acting drugs for chronic pain in osteoarthritis (OA) of the knee.

Objectives: To study the efficacy of Pregabalin in treatment of chronic pain in patients with knee OA.