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.

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Disclosure of Interest: C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. Gibofsky Shareholder of: AbbVie, Amgen, Johnson and Johnson, GSK, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Iroko, Celgene, Novartis/Sandoz, Samumed, LLC, Speakers bureau: AbbVie, Celgene, Pfizer, N. Lane Consultant for: Samumed, LLC, T. McAlindon Grant/research support from: Samumed, LLC, Consultant for: Samumed, LLC, Astellas, Flexion, Pfizer, Regeneron, Seikugaku, M. Hochberg Consultant for: Bioberica, EMD Serono, Novartis Pharma AG, Plexxikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, Theralogix LLC

DOI: 10.1136/annrheumdis-2018-eular.6036

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 not 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

DOI: 10.1136/annrheumdis-2018-eular.5215

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.

Methods: The study involved 60 female patients with knee OA having neuropathic pain component (NPC; DN4 >4). Mean age 59.82±4.46 y (min 49, max 65 years). All patients were randomly divided into two groups to be treated with 2 therapeutic regimens: aceclofenac +pregabalin (Group I) or aceclofenac (Group II) for 5 weeks (3 visits). All patients were subjected to clinical and neurological examination, total WOMAC score assessment, verification of neuropathic pain (NP) (questionnaire DN4 and Pain DETECT), and VAS pain intensity assessment at rest.

Results: The therapy was successful in both groups with respect to WOMAC score [figure 1] (Group I – 1385,30±365,83 vs 1034,70±402,37 vs 886,64±456,31; Group II – 1206,04±358,72 vs 1016,45±428,52 vs 976,55±408,02 respectively, p=0.01). Significant reduction of pain intensity at rest was documented in both groups [figure 2]. Group I 61,60±14.91 vs 45,34±16,14 vs 36,24±18,09; Group II 56,07±22,58 vs 44,86±18,68 and vs of 41.96±of 24.04, p=0.01, respectively). Therapeutic regimens in both groups had positive impact on NPC based on DN4 questionnaire and Pain DETECT scores. However, a combination of a NSAID with anticonvulsants agent (pregabalin) resulted in a more pronounced effect. Changes in DN4 values in Group I (visit1/visit3) were: 5.97±1,24/2,97±1,83 p=0.001; and in Pain DETECT values – 17,93±3,87/9,34±6,18, p=0.001; while in Group II DN4 scores were 5,35±0,93/3,79±2,29, p=0.001; and Pain DETECT – 15,03±5,26/12,24±6,29 p=0.02. [figures 3–4]

Conclusions: Complex therapy with the use of Pregabalin in patients with OA of the knee, with signs of NPC, allows not only effectively reduce pain intensity and improve functional activity of patients and, consequently, the quality of life.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2377

FRI0537 NEUROPHYSIOLOGICAL DATA IN PATIENTS WITH CHRONIC PAIN IN KNEE OSTEOARTHRITIS

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Background: Traditionally, chronic pain in OA is considered to be a classical model of nociceptive pain. Nociceptive mechanism can't explain the presence: referred pain, secondary hyperalgesia and other sensitive phenomena.¹ Recent studies has shown that besides nociceptive pain there is another mechanism that takes place in chronic pain OA –central sensitisation.² Explored of chronic pain OA can be reached only by a complex approach in examining patients with chronic knee OA that includes not only a rheumatological examination, but examination of the neurological sphere and algometry. At the moment there are only few studies dedicated to neurophysiological changes in pain OA.³

Objectives: to assess pain system with neurophysiological examination in chronic pain OA

Methods: 46 chronic knee pain OA and 23 healthy group control women, 45–65 years old, were included. The study included clinical rheumatologic, neurological examinations, neuropathic pain scales (DN4 and Pain DETECT). Knee X-ray and

ultrasound studies. Neurophysiological examination included algometry with algometer and wind-up phenomena observed by Neuropen. Five test sites in the peripatellar region and one control site on tibialis anterior (5 cm distal to the tibial tuberosity) were located and marked for examination

Results: Neuropathic pain scales demonstrated neuropathic descriptors present in OA patients. Neurological examination revealed no somatosensory deficit. But examination of the sensitive sphere indicated hyperalgesia: primary hyperalgesia (increased sensitivity to pain in the damaged joint) and secondary hyperalgesia. Algometry revealed low pressure pain threshold (PPT) above injured knee and intact region compared with healthy group. (tab.1) PPT in intact region was compared between OA patients and control group by ROC-analysis. Max of PPT in intact region in patient with OA was –14,70, min – 1,80, mean value – 7,34. Mean value of PPT in control group was 15,18. Area under curve was – 0888. Sensitivity – 70%. Specificity – 83%. ROC-analysis demonstrated that low PPT in OA patients is a specific feature of central sensitisation (figure 1) Wind-up phenomena examination in intact region revealed significant difference of data in OA patients with referred pain and control group (4,3±2,1 vs 2,44±1,3 p=0,003) and OA patients without referred pain and control group (3,67±1,43 vs 2,44±1,3 p=0,011).

PPT data	OA patients n=46	Control group n=23	P
V1	7,04±2,92	15,13±5,08	0000
V2	8,41±4,39	14,86±4,5	0001
V3	7,75±3,45	16,08±4,97	0000
V4	4,57±2,2	11,27±4,98	0000
V5	4,41±2,1	10,7±4,8	0000
V6	7,34±3,66	15,18±5,07	0000

Diagonal segments are produced by ties.

Figure 1 Diagonal segments are produced by ties.

Conclusions: Chronic OA is a complex of mechanisms and includes nociceptive and central sensitisation. Neurophysiological changes: low ppt in damaged area and even intact region and wind-up phenomena were revealed in all OA patients and characterises central sensitisation. Mechanism-oriented treatment should also target CNS, including anticonvulsant, and antidepressant agents.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1943