75.07±13.8, WOMAC pain score was 16.1±3.6. Eighty-two patients of 161 (50.9%) had neuropathic pain. When diabetics were excluded (n=58), the proportion of patients with neuropathic pain reduced to 45.6%. The most frequently described pain characteristic was sensation of electric shock (58.4%). Mean total WOMAC and physical function subscale was significantly higher in neuropathic pain group when compared to no neuropathic pain group (DN4 score 3 or less), 77.5±11.5 versus 72.6±15.5, p=0.024; and 54.3±8.8 and 49.8±12.6 respectively, p=0.008

Conclusions: Neuropathic pain was seen in up to 50% patients with knee OA. Centrally acting drugs like tricyclic anti-depressants or duloxetine can be used to improve pain and physical function in patients of knee OA with neuropathic pain.

References:

[1] Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27(6):1513–1517.

[2] Havelin J, Imbert I, Cormier J, Allen J, Porreca F, King T. Central sensitization and neuropathic features of ongoing pain in a rat model of advanced osteoarthritis. J Pain 2016; 17: 374–82.

[3] Cruccu G, Truini A. Tools for Assessing Neuropathic Pain. PLoS Med 2009; 6(4): e1000045. [Internet] http://journals.plos.org/plosmedicine/article ?id=10.1371/journal.pmed.1000045.

[4] Chopra A, Lavin P, Patwardhan B, Chitre D. A 32 week randomized, placebo controlled evaluation of RA-11, an Ayurvedic drug, on osteoarthritis of the knees. Clin Rheumatol 2004; 10:236–245.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6192

SAT0551 INCREASED SERUM AND SYNOVIAL LEVELS OF MIDKINE ARE ASSOCIATED WITH RADIOLOGICAL PROGRESSION IN KNEE OSTEOARTHRITIS PATIENTS

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Background: Midkine is a heparin-binding growth factor that plays an important role in mesoderm remodeling as in chondrogenesis and adipocyte formation. There is an increased expression of midkine in damaged tissues and it is believed to have functional antagonism, as it helps in tissue repair and survival while, on the other hand it can enhance inflammatory reactions resulting in more tissue injury [1].

Objectives: This study aimed to determine serum and synovial fluid (SF) levels of midkine in patients with primary knee osteoarthritis (KOA) and to examine the relationship between these levels with the clinical and functional parameters as well as radiological progression of KOA.

Methods: We measured midkne in the serum (n=52) and SF samples (n=23) from 52 KOA patients as well as in the serum from 20 healthy control (n=20). In the patients, numerical rating scale of pain (NRSP), body mass index (BMI) and The Western Ontario Mc Master scale (WOMAC) were recorded. Graded plain radiographs using Thomas score, and musculoskeletal ultrasound examination (MSUS) of both knees were performed at baseline and after 24 months to assess radiological progression [2,3]. Radiological progression was considered if there is an increase in the Thomas grading score or MSUS transition to a higher grade at the 24 months follow up period compared to baseline evaluation.

Results: Serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.6±14.76 pg/mL),$p<0.05$ and $p<0.001$ respectively. In KOA patients, the serum and SF concentrations of midkine significantly correlated with the baseline thickness of the cartilage on the medial condyle ($r= -0.41$ and -0.52 respectively, $p<0.05$) but not on the lateral condyle of the femur ($r=0.12$ and 0.15 respectively, $p>0.05$). Patients with elevated serum and SF midkine (defined as midkine level more than the mean plus 2 standard deviation of healthy controls's level) had a twofold increased risk of radiological progression with MSUS (age, sex and BMI adjusted RR 2.4 and 2.6, 95% CI respectively).With elevated serum and SF midkine levels, there was no increased risk of radiological progression detected with plain radiography in KOA Patients (age, sex and BMI adjusted RR 1.3 and 1.6, 95% CI respectively).

Conclusions: Osteoarthritis patients have significantly elevated serum and synovial levels of midkine that were obviously associated with radiological progression on MSUS suggesting that it could be a useful marker to reflect OA severity and implies a possible role in the pathogenesis of OA.

References:

[1] Muramatsu T. Midkine and pleiotrophin: two related proteins involved in development, survival, inflammation and tumorigenesis.J Biochem. 2002 Sep;132(3):359–71.

[2] Naredo E, Acebes C, Möller I, Canillas F, de Agustín JJ, de Miguel E, et al. Ultrasound validity in the measurement of knee cartilage thickness. Ann Rheum Dis 2009;68:1322–7.

[3] Saarakkala S, Waris P, Waris V, Tarkiainen I, Karvanen E, Aarnio J, et al. Diagnostic performance of knee ultrasonography for detecting degenerative changes of articular cartilage. Osteoarthritis Cartilage 2012;20:376–81.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5439

SAT0552 CLINICAL OUTCOMES FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, INTRA-ARTICULAR, INJECTABLE, WNT PATHWAY INHIBITOR (SM04690) FOR THE TREATMENT OF KNEE OSTEOARTHRITIS: WEEK 26 INTERIM ANALYSIS

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Background: Knee osteoarthritis (OA) is characterized by pain, disability and joint deformity due to degradation of articular cartilage and bone remodeling. The Wnt signaling pathway has a role in these cellular processes, and it is also linked to inflammation. SM04690, a small molecule Wnt pathway inhibitor, is in development for the treatment of knee OA as a potential disease modifying drug. A phase 2, multicenter, 52-week, randomized controlled trial of a single intra-articular (IA) injection of SM04690 is ongoing in subjects with moderate to severe knee OA. Clinical results from an interim analysis are reported.

Objectives: To evaluate clinical outcomes from the treatment of moderate to severe knee OA by SM04690.

Methods: Subjects with ACR defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received a 2 mL injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or placebo in the target (most painful) knee. Clinical outcomes (Western Ontario and McMaster Universities Arthritis Index [WOMAC], patient global assessment [PTGA], physician global assessment [MDGA]), were assessed at 4, 13 and 26 weeks by analysis of covariance adjusted for subject baseline in the intention-to-treat (ITT) population and two subgroups: 1) with unilateral knee OA (pre-specified); 2) without chronic pain (Widespread Pain Index [WPI]≤4, post-hoc).

Results: 455 subjects (average age 60.3 [±8.7], female 58.9%, average BMI 29.9 [±4.6] kg/m^2, KL 3 [64.4%], and bilateral OA [64.0%]) were enrolled. SM04690 appeared well tolerated. In the ITT population clinically meaningful improvements in all clinical outcomes compared to baseline were seen for all groups and placebo at weeks 13 and 26 (Table). Moreover, clinically meaningful improvements in clinical outcomes were also seen in multiple groups over several outcomes at various time points compared to placebo. In the unilateral knee OA subgroup, PTGA (0.03 mg) and MDGA (0.07 mg) were significantly improved compared to placebo. In the WPI≤4 subgroup, WOMAC Pain (0.07 mg), PTGA (0.03 mg) and MDGA (0.07 mg) were significantly improved compared to placebo.

Table. Mean (SD) Baseline and Change in Clinical Outcomes over Time by Treatment Groups

All Subjects (ITT)	Timepoint	0.03 mg	0.07 mg	0.23 mg	Placebo
n*		106	114	103	105
WOMAC Pain [0-50]	*Baseline*	25.9 (8.3)	25.9 (8.2)	25.6 (7.7)	26.0 (7.6)
	Week 13	-11.9 (11.3)	-11.8 (11.2)	-10.8 (11.4)	-11.1 (11.1)
	Week 26	-12.4 (12.0)	-13.7 (10.8)	-12.0 (10.6)	-12.1 (10.8)
WOMAC Function [0-170]	*Baseline*	90.7 (28.7)	92.3 (25.7)	88.2 (28.9)	90.4 (25.4)
	Week 13	-41.6 (37.4)	-44.2 (36.4)	-38.7 (37.7)	-39.0 (37.7)
	Week 26	-43.3 (38.4)	-48.4 (37.0)	-41.3 (36.0)	-43.5 (36.3)
Physician Global [0-100]	*Baseline*	52.7 (20.0)	53.2 (18.4)	53.0 (20.5)	52.0 (18.2)
	Week 13	-23.2 (25.1)	-26.0 (23.5)	-23.3 (25.5)	-20.8 (25.8)
	Week 26	-25.3 (28.9)	-26.8 (23.6)	-25.6 (25.8)	-21.5 (24.8)
Patient Global [0-100]	*Baseline*	45.4 (22.0)	45.3 (20.5)	45.2 (20.9)	44.1 (21.1)
	Week 13	-18.5 (24.1)	-13.8 (24.8)	-15.0 (26.8)	-13.9 (24.1)
	Week 26	-21.7 (24.7)	-17.9 (25.2)	-17.8 (27.2)	-15.9 (27.4)
Unilateral Subjects (ITT)	**Timepoint**	**0.03 mg**	**0.07 mg**	**0.23 mg**	**Placebo**
n*		43	35	42	34
WOMAC Pain [0-50]	*Baseline*	25.5 (8.5)	24.3 (8.9)	24.5 (7.1)	27.0 (7.1)
	Week 13	-13.7 (11.1)	-11.7 (8.7)	-11.7 (12.0)	-12.6 (10.7)
	Week 26	-13.7 (11.9)	-13.7 (7.9)	-12.3 (10.6)	-11.7 (10.1)
WOMAC Function [0-170]	*Baseline*	92.7 (29.6)	85.3 (27.7)	84.2 (28.6)	91.2 (22.7)
	Week 13	-51.3 (34.9)	-44.8 (28.7)	-39.7 (40.7)	-39.7 (39.3)
	Week 26	-50.5 (39.5)	-47.6 (28.0)	-42.7 (38.0)	-40.8 (34.2)
Physician Global [0-100]	*Baseline*	54.5 (18.5)	50.6 (20.5)	52.8 (24.2)	50.5 (17.8)
	Week 13	-30.6 (24.6)†	-25.6 (19.7)	-24.5 (27.1)	-17.4 (26.5)
	Week 26	-29.2 (29.8)	-27.6 (25.7)†	-27.9 (24.6)	-17.4 (25.9)
Patient Global [0-100]	*Baseline*	44.2 (23.1)	44.3 (24.1)	48.8 (19.7)	45.7 (19.9)
	Week 13	-22.9 (24.0)†	-13.3 (24.3)	-20.0 (28.1)	-13.8 (24.4)
	Week 26	-26.8 (23.6)‡	-20.4 (29.1)	-20.2 (30.4)	-13.8 (31.0)
WPI ≤ 4 (ITT)	**Timepoint**	**0.03 mg**	**0.07 mg**	**0.23 mg**	**Placebo**
n*		64	66	63	64
WOMAC Pain [0-50]	*Baseline*	25.6 (7.4)	25.5 (8.7)	26.7 (5.8)	26.5 (7.0)
	Week 13	-13.4 (11.3)	-12.2 (11.5)	-11.6 (11.9)	-11.0 (11.6)
	Week 26	-12.4 (12.0)	-14.8 (11.1)†	-12.9 (10.5)	-11.5 (11.2)
WOMAC Function [0-170]	*Baseline*	90.6 (25.6)	88.7 (26.7)	93.6 (21.5)	91.1 (24.9)
	Week 13	-47.6 (39.2)	-44.0 (35.7)	-43.4 (36.2)	-35.9 (39.7)
	Week 26	-46.1 (41.2)	-49.8 (36.9)	-46.6 (34.2)	-39.5 (36.4)
Physician Global [0-100]	*Baseline*	53.2 (19.5)	53.4 (19.7)	56.9 (18.6)	51.6 (18.1)
	Week 13	-24.8 (25.7)	-26.1 (24.4)	-24.9 (27.5)	-18.7 (26.9)
	Week 26	-24.5 (29.6)	-28.4 (25.2)‡	-26.2 (27.3)	-18.0 (24.9)
Patient Global [0-100]	*Baseline*	44.3 (23.0)	43.9 (23.7)	47.8 (22.4)	42.8 (21.1)
	Week 13	-21.6 (24.9)‡	-15.1 (26.7)	-18.1 (28.6)	-12.1 (26.2)
	Week 26	-23.8 (25.7)†	-21.1 (27.6)	-21.1 (28.6)	-14.3 (29.1)

*Ns represent observations at Week 26.†P<0.05 compared to placebo. ‡ P<0.01 compared to placebo.

Conclusions: In this phase 2 interim analysis, the ITT population (SM04690 and placebo groups) demonstrated clinically relevant improvements in clinical outcomes at weeks 13 and 26 compared to baseline. In two subgroups, consistent

improvements over placebo were seen in 0.03 mg and 0.07 mg treatment arms, achieving statistical significance for PTGA and MDGA. Further studies to identify relevant sub-populations and evaluate the safety and efficacy of SM04690 are ongoing.

Disclosure of Interest: Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. Gibofsky Shareholder of: AbbVie, Amgen, J&J, GSK, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Iroko, Celgene, Novartis/Sandoz, Samumed, Speakers bureau: AbbVie, Amgen, Celgene, Pfizer, N. Lane Consultant for: Samumed, LLC, N. Skrepnik Grant/research support from: Samumed, LLC, Consultant for: Orthofix and Sanofi, E. Armas Grant/research support from: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. DiFrancesco Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. McAlindon Grant/research support from: Samumed, Consultant for: Astellas, Flexion, Pfizer, Regeneron, Samumed,and Seikugaku

DOI: 10.1136/annrheumdis-2017-eular.6382

SAT0553 DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTIENASE-13 AND INTER LEUKIN-1 BETA DURING REMISSION AND FLARE-UPS OF PRIMARY OSTEOARTHRITIS OF THE KNEES

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Background: The diagnosis of osteoarthritis is currently based on radiographic criteria (eg, joint space width) and clinical symptoms (eg, pain and loss of function).

The evaluation of new disease-modifying osteoarthritis drugs (DMOADs) is performed on the same basis, since the regulatory bodies currently require evidence for an impact on radiographic joint space narrowing (JSN) and an impact on symptoms However, the limitations of radiography have led to research into alternative parameters for monitoring osteoarthritis that could serve as biomarkers in drug development.

Objectives: Detection the serum level of MMP-13 and IL-1 β In OA of the knee during remission and exacerbation and if these Biomarkers can be validated as gold biomarkers in assessing OA progression and drug development in OA treatment.

Methods: This study was performed on 60 patients with knee osteoarthritis, 18 males (30%) and 42 females (70%), all diagnosed as osteoarthritis of one or both knees. Their ages ranged from (40 -65) years. The duration of their disease ranged from one to 15years. The control groups were 8 males (32%) and 17 females (68%). their ages ranged from (40–65) years.

- The patients were allowed to continue on the medications that they have pro inflammatory cytokines (IL-1β) and degradative enzymes (MMP-13) are measured.
- Clinical assessing for pain using visual analogue scale (0–10)
- Assessing for pain, stiffness and physical functions by:
  (A) the WOMAC osteoarthritis index
  (B) Lequesne's algo functional index
- Asssesing the flare-ups using Knee Osteoarthritis Flare Ups Score (KOFUS).

Results: Patients who had 3 flare-ups (during one year follow up) showed the statistically significantly highest mean IL-1β & MMP13 level.

There was no statistically significant difference between patients with no flare-up, 1 flare-up and 2 flare-ups; all showed statistically significantly lower mean levels.

There was a statistically significant positive (direct) correlation between IL-1β, disease duration, KL, VAS, stiffness score, pain score, functional score, WOMAC and KOFUS. An increase in all these variables is associated with an increase in IL-1β & MMP13.

Conclusions:

- There is a potential role for IL1 beta and MMP 13 biomarkers in assessing the development in osteoarthritis.
- IL 1 β and MMP 13 were founded to be correlated positively in patients with knee OA this correlation sounded right as the expression of MMP 13 depends on the level of IL1 β.
- Although all medications groups failed to lower the level of IL 1 β and MMP 13,yet there was a numerical difference in favor of Diacerine and NSAID.
- patients on both Diacerine and NSAID had the lowerest rate of flare ups
- It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1134

SAT0554 INVESTIGATION OF SELECTED BIOCHEMICAL MARKERS IN KNEE OSTEOARTHRITIS: THE FRAMINGHAM OSTEOARTHRITIS COHORT

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Background: Osteoarthritis (OA) is a major cause of functional impairment and disability among the elderly. There is an unmet need for the development of biomarkers for identifying patients with high risk for OA and for monitoring drug efficacy. Specific and sensitive biochemical markers revealing the turnover of bone, cartilage, and synovial tissue may be useful for investigation and monitoring of OA.

Objectives: To investigate a targeted set of five biochemical markers, which reflect joint tissue turnover, for their ability to evaluate the prevalence of radiographic and symptomatic knee osteoarthritis (OA) in a substudy from the cross-sectional Framingham OA cohort (FOA).

Methods: The subjects from the community-based FOA cohort were divided up based on a terminology proposed by the FNIH-OAI consortium. Two main groups were defined: subjects with radiographic knee OA (RKOA, n=80) and a group with no radiographic OA (NRKOA, n=136). The presence of ROA as any Kellgren-Lawrence (KL) grade =2 or 3. The RKOA group were further divided into two groups; those with persistent symptoms of a joint (RKOA+S, n=30) and those without (RKOA-S, n=50). +S was defined as having pain, aching or stiffness in either knee on most days.

Serum levels of C1M, CRPM and huARGS (matrix metalloproteinases cleaved type I collagen and C-reactive protein neo-epitopes, aggrecanase cleaved ^{374}ARGS neoepitope of aggrecan, Nordic Bioscience) were determined by ELISA. Serum levels of cartilage synthesis and degradation biomarkers, hsPro-C2 and hsAGNx-1 (procollagen type IIB N-terminal propeptide, aggrecanase cleaved TEGE^{373} neoepitope of aggrecan, Nordic Bioscience) were measured by electrochemiluminescence immunoassay (ECLIA). Each measure was fisher transformed in order to be comparable across the biomarkers. The correlation between the biomarkers and covariates was assessed.

The subjects of substudy were segregated into two groups based on the cut-off values of each biomarker. The cut-off values of these markers were set as mean of their reference levels. We used logistic regression to compare these two groups, and to examine the association between each marker and the presence of OA and/or pain. All confounding factors were adjusted.

Results: The two main groups were well-matched by age, sex, and BMI. Two biomarkers correlated negatively with BMI: C1M and CRPM. Aggrecan degradation biomarker, hsAGNx-1 was negatively associated with age while the huARGS was not associated with it (Table 1).

CRPM was associated with a lower risk of RKOA+S. Interestingly, hsPro-C2 was associated with a higher risk of it (Table 2).

Table 1. Subject characteristics of substudy

Covariates	NRKOA (n=136)	RKOA-S (n=50)	RKOA+S (n=30)	Biomarker (Fisher transformed) associations with covariates
BMI, mean kg/m^2 (SD)	31.3 (3.79)	32.3 (6.05)	31.6 (5.12)	C1M, CRPM
WOMAC pain	0.182 (0.657)	0.820 (1.66)	4.83 (3.64)	
Age, mean years (SD)	62.6 (8.18)	63.7 (7.06)	62.4 (7.09)	hsAGNx-1
Sex, n (%) female	82 (60.3%)	33 (66.0%)	18 (60.0%)	C1M

Table 2. Odds ratio of OA in the substudy. Values in bold represent associations of p≤0.05. OR data are for each definition of OA, using logistic regression and adjusted for age, sex, and BMI (Upper: unadjusted, Lower: adjusted). ORs are for comparison with knees with NRKOA subjects.

Biomarker	OR of RKOA-S (95% CI)	OR of RKOA+S (95% CI)
C1M	1.07 (0.54 - 2.10)	0.47 (0.18 - 1.24)
CRPM	0.97 (0.51 - 1.88)	0.41 (0.16 - 1.02)
hsAGNx-1	1.20 (0.61 - 2.38)	0.68 (0.27 - 1.72)
hsPro-C2	1.27 (0.63 - 2.57)	**2.51 (1.10 - 5.73)**
huARGS	1.43 (0.71 - 2.88)	1.19 (0.50 - 2.84)
Biomarker	**OR of RKOA-S (95% CI)**	**OR of RKOA+S (95% CI)**
C1M	0.96 (0.47 - 1.95)	0.45 (0.17 - 1.20)
CRPM	0.87 (0.44 - 1.71)	**0.39 (0.16 – 1.00)**
hsAGNx-1	1.11 (0.55 - 2.23)	0.68 (0.27 - 1.72)
hsPro-C2	1.32 (0.64 - 2.72)	**2.55 (1.11 - 5.82)**
huARGS	1.49 (0.73 - 3.03)	1.21 (0.50 - 2.92)

Conclusions: This study provides two major findings: 1) aggrecan degradation is not just aggrecan degradation and different neo-epitopes have distinct clinical relevance; 2) CRPM is a candidate biomarker of disease activity and for patient profiling. These data suggest a reference for interpretation of OA subject biomarker data in future human studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1744

SAT0555 MRI-DETECTED KNEE OSTEOPHYTE: NATURAL HISTORY AND STRUCTURAL RISK FACTORS AFFECTING CHANGE

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Background: Although magnetic resonance imaging (MRI) has been proved to be far more sensitive than conventional radiographs to detect OP, the natural history of MRI-detected OP in older adults has not yet been described, and it is unclear whether knee structural abnormalities, including cartilage defects, cartilage volume, bone marrow lesions (BMLs), meniscal extrusion, infrapatellar fat pad (IPFP), and effusion-synovitis, can predict osteophyte change.

Objectives: To describe the natural history of knee MRI-detected OP, and to determine if knee structural risk factors are associated with change of MRI-detected OP in a longitudinal study of older adults.