Investigation Of Selected Biochemical Markers In Knee Osteoarthritis: The Framingham Osteoarthritis Cohort

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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.


SAT0553 DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTEINASE-13 AND INTER LEUKIN-1BETA 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-1β 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
• Assessing 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, 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.

Conclusions: There is a 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 IL 1 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 Dicacieme and NSAIAD.
• patients on both Dicacieme and NSAIAD had the lowest 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

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SAT0554 INVESTIGATION OF SELECTED BIOCHEMICAL MARKERS IN KNEE 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 cartilage 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 an radiographic knee OA (ROKA, n=80) and a group with no radiographic OA (NROKA, n=136). The prevalence of ROA as any Kellgren-Lawrence (KL) grade ≥2 or 3. The ROKA group were further divided into two groups; those with persistent symptoms of a joint (ROKA+S, n=30) and those without (ROKA−, n=50). The cut-off was defined as having pain, aching or stiffness in either knee on most days.

Serum levels of C1M, CRPMA and huARGS (matrix metalloproteinases cleaved type I collagen and C-reactive protein neo-epitopes, aggrecanase cleaved 13403926 neoepitope of aggrecan, Nordic Bioscience) were determined by ELISA. Serum levels of cartilage synthesis and degradation biomarkers, hPro-C2 and hSAGNx-1 (procollagen type IIB N-terminal propeptide, aggrecanase cleaved TEGE373 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 subgroups was assessed. The subjects of study 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 hARGS was not associated with it (Table 1). CRPM was associated with a lower risk of ROKA+S. Interestingly, hPro-C2 was associated with a higher risk of it (Table 2).

Table 1. Subject characteristics of study group

<table>
<thead>
<tr>
<th>Covariates</th>
<th>NROKA</th>
<th>ROKA-S</th>
<th>ROKA-S</th>
<th>Biomarker (Fishers transformed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, mean kg/m² (SD)</td>
<td>31.3 (7.99)</td>
<td>32.3 (6.36)</td>
<td>31.5 (8.12)</td>
<td>C1M, CRPM</td>
</tr>
<tr>
<td>WOMAC pain</td>
<td>0.182 (0.657)</td>
<td>0.620 (1.66)</td>
<td>0.83 (3.64)</td>
<td>hPRO-C2 &amp; MMP13</td>
</tr>
</tbody>
</table>

Table 2. Odds ratios of OA in the subgroups. Values in bold represent associations of p < 0.05. OD ratios for each definition of OA using logistic regression and adjusted for age, sex, and BMI unless otherwise stated. ORs are for comparison with OA enrollee with subgroups.

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

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