and OA towards the incident comorbidity was estimated using addictive interaction methods. We also investigated the individual risk across non-selective, and COX-2 selective NSAIDs.

Results: The mean age was 59.4±12.8 years in people with OA and 60.2±12.8 years for controls with 57.7% being female. Nearly two thirds of people with OA were prescribed NSAIDs as defined, compared to one third in the control population. People with OA and exposed to NSAIDs had highest risk of developing psychological (1.51; 1.43,1.60), CVD (1.38; 1.33,1.43), cancer (1.34; 1.25,1.44), GI (1.25; 1.16,1.34) and renal (1.17; 1.11,1.24) comorbidities after adjusting for all the covariates and PPI drugs, compared to the non-OA and non-NSAID group. (Figure 1) Interaction between OA and NSAID was significant for cancer, GI, renal, hepatic, and neurological outcomes. Within people with OA, non-selective NSAIDs increased the risk of CVD (1.25; 1.20,1.30), cancer (1.11; 1.04,1.19), endocrine (1.15; 1.10,1.19), renal (1.19; 1.13,1.26) and psychological (1.21; 1.15,1.28) comorbidities, whereas COX-2 selective NSAIDs increased risk of incident CVD (1.34; 1.25,1.44), endocrine (1.13; 1.04,1.21), renal (1.25; 1.14,1.37), and psychological (1.21; 1.09,1.34) comorbidities.

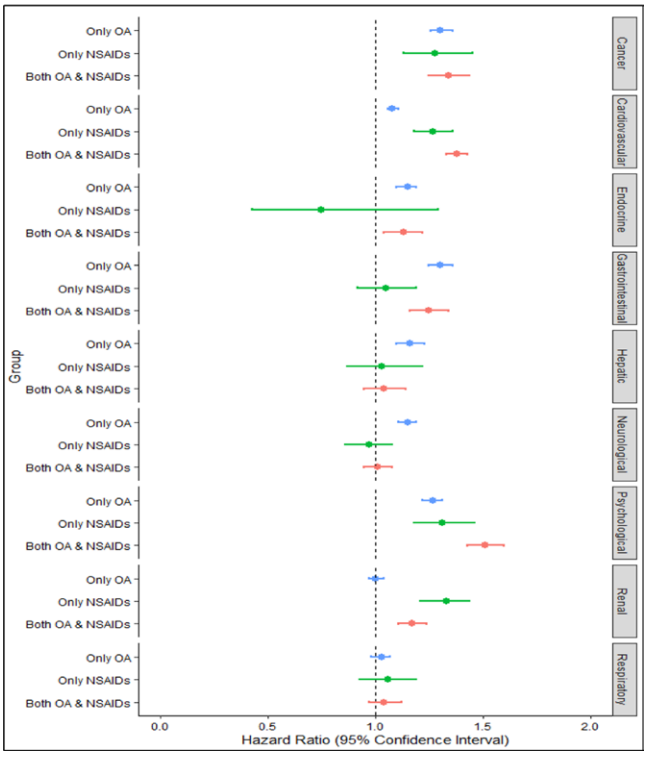

Figure 1. Hazard ratio of developing different comorbidities (reference group: no OA and no NSAIDs) OA- Osteoarthritis; NSAIDS- Non-steroidal anti-inflammatory drugs.

Conclusion: Use of NSAIDs among people with OA is associated with increased risk of a wide variety of comorbidities. Non-selective and COX-2 selective NSAIDs are both associated with increased risk of cardiovascular, renal, and psychological comorbidities.

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OP0229

OSTEOARTHRITIS OF THE KNEE, INFLAMMATION, AND THE EFFECT OF ADALIMUMAB (OKINADA): A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Background: Cytokines such as tumor necrosis factor (TNFα) have been shown to elicit inflammatory and catabolic events in the joints of patients with osteoarthritis. Recent RCTs demonstrated that TNFα inhibition has no effect on pain and MRI-detected synovitis or bone marrow lesions in patients with erosive hand OA[1-3]. However, the progression of bone erosions was reduced in a subgroup of patients with more clinically swollen distal interphalangeal joints in one RCT[1]. Consequently, it remains possible that TNFα inhibition may have beneficial effects in specific subgroups of patients with a high inflammatory component.

Objectives: We aimed to evaluate the efficacy and safety of a TNFα inhibitor, adalimumab (ADA), in a proof-of-concept study in patients with inflammatory OA of the knee.

Methods: OKINADA was a 52-week, randomized, double-blind, placebo-controlled, parallel-group study done at 11 sites in Canada (NCT02471118). Eligible participants were adults (aged ≥18 years) with a diagnosis of OA of the index knee and classified according to American College of Rheumatology criteria, including radiological evidence of OA (Kellgren-Lawrence grades 2 or 3) with clinical signs of knee effusion. Subjects had persistent knee pain of ≥ one month duration with a pain score of ≥ 4 (0-10 NRS) in the index knee at screening and baseline despite conventional treatment with maximum tolerated acetaminophen and/or non-steroidal anti-inflammatory drug. Patients were randomly assigned (1:1) to receive subcutaneous 40 mg ADA every 2 weeks or placebo (PBO). Primary endpoint was the Outcome Measures in Rheumatology and Osteoarthritis Research Society International set of responder criteria (OMERACT-OARSI) at week 16 defined as: (1) improvement in pain or function ≥50% and an absolute change ≥20 mm; or (2) improvement of ≥20% with an absolute change ≥10 mm in at least two of the following three categories: pain, function, and patient's global assessment. Secondary endpoints included: the Knee Injury and Osteoarthritis Outcome Score (KOOS) for the domains of pain, activities of daily living (ADL), OA symptoms, sport and recreation function (SRF), and knee-related quality of life (QoL), patient's global assessment of disease status (PGAD), investigator global assessment of disease status (IGAD), and expanded Target Joint Assessment (TJA) score.

Results: A total of 59 patients were randomized (29 to PBO, 30 to ADA). The primary endpoint was not met: OMERACT-OARSI combined (ADA: 9 [30.0%] vs PBO: 7 [24.1%], p=0.62). For KOOS pain, ≥20% improvement was noted in 11 (36.7%) ADA vs 7 (24.1%) PBO patients (p=0.30), and ≥50% improvement in 5 (16.7%) ADA vs 6 (20.7%) PBO patients (p=0.69). There were no significant treatment-group differences in baseline to 16-week change in continuous secondary endpoints (ADA vs PBO: KOOS ADL 6.5 vs 8.4 (p=0.71), KOOS QoL 10.1 vs 7.4 (p=0.66), KOOS symptoms 7.8 vs 11.5 (p=0.42), KOOS SRF 5.8 vs 7.7 (p=0.76), PGAD -1.0 vs 0.1 (p=0.10), IGAD -1.5 vs -2.1 (p=0.30), TJA -2.4 vs -2.2 (p=0.87) or in lab markers (ESR, CRP). There were 11 withdrawals (4 ADA, 7 PBO) of which 2 were for adverse events (1 ADA, 1 PBO) and 2 for increasing knee pain (1 ADA, 1 PBO). No new safety signals were identified and there were no serious adverse events.

Conclusion: Although the treatment was safe, short-term treatment with anti-TNFα therapy does not appear to provide clinically meaningful improvements in OA symptoms in patients with established radiographic knee OA. Analyses of structural endpoints will be reported when results are available.

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OP0230 ANTIHISTAMINE USE AND STRUCTURAL PROGRESSION OF KNEE OA: A POST-HOC ANALYSIS OF TWO PHASE III CLINICAL TRIALS

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Background: Prior studies indicate that mast cells are involved in chronic inflammation and that their activity in the synovium may contribute to structural progression of osteoarthritis (OA), however the exact role of mast cells in OA remains unclear. Antihistamines act by blocking histamine receptors, and further are found to have anti-inflammatory effects by stabilizing mast cell membranes. Current reports describing antihistamine use in OA patients suggest that antihistamines may reduce development of OA and lead to reduced risk of structural progression.

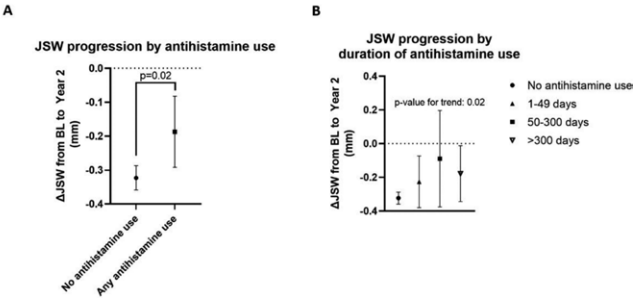
Objectives: We aimed to investigate whether antihistamine use during a two-year trial period was associated with differences in structural progression of OA, as compared with non-use.

Methods: This is a post-hoc analysis of two large phase III trials investigating oral salmon calcitonin in knee OA (NCT00486434 and NCT00704847). The primary outcome measure was structural progression defined as the change in minimum joint-space width measured by use of x-ray imaging from baseline to Year Two. In these trials, participants reported use of antihistamines, defined as medication coded with the ATC code R06A. In our study, we evaluated differences between groups of participants who reported use of antihistamines, versus those who did not, over the 2-year study period. Secondly, the duration of antihistamine use divided into categories of either no use, 1-49, 50-299 or >300 days of use was investigated to evaluate exposure-response relationships. The effect of use of antihistamines was evaluated using ANCOVA analysis adjusting for age, sex, BMI, and baseline JSW.

Results: Of a total study population of 2,206 participants, 1,485 completed the trial. Of these, 1,327 were non-users of antihistamines (mean age 64.4 years, 64.1% female, mean BMI 29.0 kg/m^2) and 158 reported use of antihistamines of any duration during the trial (mean age 64.5 years, 75.2% female, mean BMI 28.1 kg/m^2). Seventy-four participants reported use of antihistamines of a duration between 1-49 days, 21 participants between 50-299 days, and 63 reported use of 300 days or more. As illustrated in Figure 1A, the mean JSW change from baseline in the group of non-users was -0.32 mm (95% CI: -0.36 to -0.29), versus -0.19 mm (95%CI: -0.29 to -0.08, p=0.02 for difference) in the group of patients reporting antihistamine use of any duration. A trend towards an association between duration of antihistamine use and reductions in narrowing of JSW was observed (p for trend: 0.02), Figure 1B).

Conclusion: Use of antihistamines was associated with reduced structural progression in knee OA. Further research evaluating the role of antihistamines in OA is needed to further characterize this observation.

FIGURE 1



Disclosure of Interests: Asger Reinstrup Bihlet Shareholder of: Shareholder of NBCD A/S, Employee of: Employee at NBCD A/S, Claire Prener Miller Employee of: Employee at NBCD A/S, Inger Byrjalsen Employee of: Past employee at NBCD A/S, Jeppe Ragnar Andersen Shareholder of: Shareholder of NBCD A/S, Employee of: Employee at NBCD A/S, Morten Karsdal Shareholder of: Shareholder of Nordic Bioscience A/S, Employee of: Employee at Nordic Bioscience A/S, Matthew C. Baker Shareholder of: Shareholder of Mobility Bio Inc., Employee of: Employee at Mobility Bio Inc., Tharaknath Rao Shareholder of: Shareholder of Mobility Bio Inc., Employee of: Employee of Mobility Bio Inc.

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Novel etiopathogenic aspects in SLE and Sjögren's sydrome

OP0231 MASS CYTOMETRY DATA RECLASSIFY SYSTEMIC AUTOIMMUNE DISEASE PATIENTS IN PHENOTYPICALLY DISTINCTIVE GROUPS

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Background: Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSC), Sjögren's syndrome (SJS), mixed connective tissue disease (MCTD), primary antiphospholipid syndrome (PAPS) and undifferentiated connective tissue disease (UCTD) are classified as systemic autoimmune diseases (SADs). They are diagnosed based on different clinical and laboratory criteria. Due to their high internal heterogeneity and overlapping symptoms, SADs are difficult to diagnose. Therefore, molecular and cellular-based studies need to be undertaken to precisely classify the patients. Mass cytometry is a single-cell proteomics technology that measures approximately 50 markers per cell, thus it is a suitable tool to perform deep-phenotyping studies in SADs.

Objectives: Explore differences and similarities between SADs and build reclassification framework using high-dimensional cytometry data.

Methods: The whole blood samples collected from 129 individuals, including patients and controls were stained with a 39-plex antibody panel and acquired