BIOMARKERS PREDICTIVE OF PAIN IMPROVEMENT IN KNEE OSTEOARTHRITIS SUBJECTS TREATED WITH THE ANTI-IL-1 ALPHA/IL-1BETA DUAL VARIABLE DOMAIN IMMUNOGLOBULIN LUTIKIZUMAB (ABT-981)

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Background: Development of disease-modifying drugs for OA has been challenging, partly due to lack of predictive biomarkers.

Objectives: Our primary objective was to identify baseline (BL) biomarkers predicting greater treatment effects on WOMAC pain among knee OA subjects in the lutikizumab (formerly ABT-981) ILLUSTRATE-K trial (NCT02087904).

Methods: Subjects (n=347) with Kellgren-Lawrence (KL) grade 2–3 knee OA, synovial inflammation (SynOx score ≥2), and knee pain scores 4–9 (range, 0–10) were randomized to placebo (PBO) or lutikizumab 25, 100, or 200 mg subcutaneously every 2 wk for 52 wk. The primary endpoints were change from BL in WOMAC pain at wk 16 and CFB in MRI synovitis at wk 26. Demographic, patient-reported outcomes (WOMAC, IQoP, global assessment [PGA]), x-ray joint space width, and Whole Organ MRI Score (WORMS) were determined at BL. The Patient Rule Induction Method, Sequential Bating, and the Adaptive Index Model were used to identify BL predictive biomarkers and OA subsets with greater lutikizumab treatment effects. Continuous efficacy endpoints were assessed using ANCOVA with treatment, age group, and KL grade as main factors and BL measurements as covariates with LOCF imputation for WOMAC pain.

Results: WOMS Global Total Osteophyte Score (GTOS), which semi-quantitatively summarizes osteophyte severity from 14 regions of the knee, identified a subset of subjects with a greater lutikizumab treatment effect vs PBO; the optimal GTOS cutoff for discriminating treatment effects was 14 (figure 1). Among subjects with GTOS >14, the PBO WOMAC pain response was markedly reduced and only marginally improved for ABT-981. At wk 16, among subjects with GTOS >14, the standardized mean difference (95% CI) of WOMAC pain for the lutikizumab 100 mg dose group vs PBO was −0.62 (−0.16 to −0.9) vs −0.30 (0 to −0.61) for all subjects. Compared with the total study population, the 41% of subjects with GTOS >14 not only had a greater ABT-981 treatment effect vs PBO on WOMAC pain, but also other measures of OA symptoms. BL systemic markers of synovitis (serum C1M and C3M) and potential markers of macrophage activation by IL-1 (serum alkaline phosphatase) were positively associated with greater lutikizumab treatment effects vs PBO but to a lesser extent than GTOS. Other data supported the robustness of the GTOS predictive marker because 1) a priori KL grade was used to stratify subjects, 2) subject characteristics were balanced and 3) osteophyte formation is directly linked with synovial macrophage numbers in humans and OA synovial macrophages are the predominant source of IL-1, which is an important mediator of pain.

EVALUATION OF SARCOPENIA MULTIDIMENSIONALLY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a noninflammatory chronic degenerative disease. The rate of development of sarcopenia has been increased in patients with OA.

Objectives: In this study, we evaluated the presence of sarcopenia multidimensionally in patients with knee osteoarthritis (OA) using clinical, ultrasonographic and biochemical parameters and in this respect, it was aimed to investigate the relationship between OA and sarcopenia and to identify the most practical, easily accessible and inexpensive method for investigating sarcopenia.

Methods: 102 patients with clinical and radiological diagnosis of knee osteoarthritis and 33 healthy control subjects were included in the study. A total of 135 subjects were evaluated by the European Working Group on Sarcopenia in Older People (EWGSOP) for the diagnosis of sarcopenia. The first group consists of (OA) patients with sarcopenia, the second group consist of OA patients without sarcopenia and the third group is controls subjects. Dual-X-ray absorptiometry (DEXA) is used to measure Body composition parameters and muscle mass measurements, isometric muscle strength evaluations, hand grip strength and walking speeds for diagnosis of sarcopenia. Short form – 36 (SF–36) The Nutritional Assessment-short form (MNA), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the International Physical Assessment Questionnaire Short Form (IPAQ-SF) and the Centre for Epidemiologic Studies Depression Scale (CES-D scale) were administered to every patient.

Results: The mean age of the group with sarcopenia was statistically higher than the other two groups (p<0.001). The weight, body mass index (BMI), waist circumference, hip circumference, upper mid-arm circumference, thigh and leg circumference of osteoarthritic (OA) patients with sarcopenia were statistically lower than those of non-sarcopenic and control group (p<0.01 p<0.001). Body composition parameters results showed that sarcopenic patients had statistically lower values as fat mass, lean body mass and Skeletal Muscle Index (p<0.001, p<0.001, p=0.01, respectively) than those of non-sarcopenic and control group. It was determined that body composition values measured with DEXA, ultrasonographic measures, through wk 52. Pharmacodynamic responses (neuroph and high-sensitivity CRP levels) plateaued at the 100 mg dose and similar at 200 mg. The low immunogenicity of lutikizumab did not meaningfully affect outcomes.

Conclusions: Lutikizumab was generally well tolerated and met the primary end-point of reduction in WOMAC pain at wk 16 compared with placebo at a dose of 100 mg, but not at 25 mg or 200 mg; cartilage thickness, synovitis, and other structural endpoints were similar between lutikizumab and PBO.

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isokinetic muscle strength assessment, hand grip strength and gait speed had predictive values for sarcopenia.

Conclusions: We found that patients with sarcopenic OA were older, weaker, less powerful, undernourished, and restricted in their level of physical activity in the study in which we identified sarcopenia as approximately 12% in patients with osteoarthritis. Among the methods of determining sarcopenia, ultrasound becomes prominent with its practical, cheap and easily accessible features. We think that our results will increase the awareness of the presence of sarcopenia in OA patients.

REFERENCES:

Disclosure of Interest: None declared

PATELLAR TENDON ENTHESIS ABNORMALITIES AND THEIR ASSOCIATION WITH KNEE PAIN AND STRUCTURAL ABNORMALITIES IN OLDER ADULTS

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Background: The patellar tendon works together with the quadriceps tendon to enable knee flexion and straightening. Its attachment site (enthesis) is at risk of micro damage and degeneration. Recent studies suggest that enthesis abnormalities are associated with development of osteoarthritis. 1, 2 However, no studies have assessed the presence of patellar enthesis abnormalities in older adults and its association with osteoarthritis outcomes.

Objectives: To describe the associations of patellar tendon enthesis (PTE) abnormalities visible on magnetic resonance (MR) images; and knee pain, physical function limitations, osteoarthritic structural abnormalities cross-sectionally and longitudinally over 10.7 years.

Methods: PTE abnormalities were defined as presence of abnormal bone signal and/or bone erosion. They were measured on T2-weighted fat suppressed fast spin echo MR images at baseline in 961 community-dwelling older adults and followed for 10.7 years. Knee pain and physical function limitation score were assessed using WOMAC. Bone marrow lesions (BMLs), cartilage volume and infrapatellar fat pad (IPFP) area were assessed using validated methods. Associations were assessed using hurdle, log binomial, linear, and mixed models, after adjusting for confounders.

Results: Cross-sectionally, presence of PTE abnormalities were associated with greater intensity of pain while going up and down stairs (β=0.22 (95% CI: 0.03, 0.41)), greater risk of having a femoral BML (RR=1.46 (1.22, 1.90)), greater lateral tibial bone area (β=25.95 (1.00, 50.91)), smaller IPFP area (β=-0.26 (0.46, -0.05)), and a worse tibial cartilage defect cross sectionally (RR=1.70 (1.16, 2.47), after adjustment of demographic and structural confounders. Longitudinally, PTE abnormalities at baseline predicted an increased risk of deleterious changes in tibial BML size (RR=1.52 (1.12, 2.05)) but not clinical symptoms, and other structural changes over 10.7 years.

Conclusions: Patellar tendon enthesis abnormalities are common in the elderly. The presence of cross-sectional but not longitudinal associations suggests they commonly co-exist with other knee structural abnormalities, but that they are not a major player in symptom development or structural changes, excepting tibial BMLs.

REFERENCES:

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