out strategies for pain management could improve this PCS values and therefore reduce the need for TKR. Furthermore, this study also highlights the two mainly types of OA etiology: mechanical and inflammatory. It suggests that inflammation is mostly responsible for OA progression in patients with low BMI, and plays a strong role in women pathology. Finally, specific treatments targeting central pain sensitization could also improve the management of the pathology in women.

References:

- [1] Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health*. 1994 Mar;84(3):351-8.
- [2] O'Neill TW, Felson DT. Mechanisms of Osteoarthritis (OA) Pain. *Curr Osteoporos Rep*. 2018 Oct;16(5):611-6.
- [3] Dieppe PA. Relationship between symptoms and structural change in osteoarthritis. what are the important targets for osteoarthritis therapy? *J Rheumatol Suppl*. 2004 Apr;70:50-3.

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FRI0427

EULAR RECOMMENDATIONS FOR INTRA-ARTICULAR TREATMENTS FOR ARTHROPATHIES

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Background: Intra-articular therapies (IAT) are widely used in clinical practice to treat patients with rheumatic and musculoskeletal diseases (RMDs). Many factors influence their efficacy and safety. There is a wide variation in the way IATs are delivered by health professionals. In an attempt to standardise these procedures, evidence-based recommendations are the right way forward.

Objectives: To establish evidence-based recommendations to guide health professionals using IAT in adult patients with peripheral arthropathies.

Methods: At a first face-to-face meeting, the results of an overview of systematic reviews were presented to the multidisciplinary task force of members from 8 countries. The aim, scope and outline of the taskforce were also established at this meeting. Thirty-two clinical questions ranked for priority (relevance for practice plus feasibility) drove the systematic reviews performed by two fellows. In addition, two surveys addressed to physicians, health professionals and patients throughout Europe were agreed to acquire more background information. At the second face-to-face meeting, the evidence for each research question was discussed, and each recommendation shaped and voted in a first Delphi round. Level of agreement was numerically scored 0 to 10 (0 completely disagree, 10 completely agree). All panellists voted anonymously using a sli. do app. Agreement needed to be greater than 80% to be included in a second Delphi round, which also allowed reformulation of statements. Finally, a third Delphi round was sent to the taskforce. The level of evidence was assigned to each recommendation according to the EULAR SOP for establishing recommendations.

Results: Recommendations focus on practical aspects for daily practice to guide health professionals before, during and after IAT in adult patients with peripheral arthropathies. Five overarching principles were established, together with 11 recommendations that address the following issues: (1) patient information; (2) procedure and setting; (3) accuracy issues; (3) routine and special antiseptic care; (4) safety issues and precautions to be addressed in special populations; (5) efficacy and safety of repeated joint injections; (6) the usage of local anaesthetics; and (7) aftercare. The document includes the supporting evidence and results from the surveys, level of evidence and agreement.

Conclusion: We have developed the first evidence and expert opinion based recommendations to guide health professionals using IAT.

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FRI0428

RESULTS FROM A CROSS-SECTIONAL, OBSERVATIONAL STUDY TO ASSESS INADEQUATE PAIN RELIEF IN PATIENTS WITH KNEE AND/OR HIP OSTEOARTHRITIS IN CHINA

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Background: Osteoarthritis (OA) of the knee and hip is a leading cause of disability worldwide, particularly due to the primary symptom of pain in the weight-bearing joints. There is limited data that characterizes patients who experience moderate to severe pain despite analgesic treatment in China.

Objectives: This study estimates the real-world prevalence of inadequate pain relief (IPR) among patients with knee and/or hip OA who have been prescribed analgesic therapy and characterizes this patient population. The study was conducted in China, the Philippines, Thailand, Russia, and Mexico. This abstract presents results from China.

Methods: This is a multinational, multi-site, cross-sectional, observational study. Physicians managing patients with OA were recruited and asked to enroll patients over 50 years of age with knee and/or hip OA who had been prescribed topical and/or oral pain medication for at least 30 days prior to study visit. Patients completed a one-time assessment of pain, function, and health-related quality of life (HRQOL) using patient reported outcome (PRO) instruments. Physicians abstracted data from patient charts. IPR was defined as an average pain score of >4/10 on Brief Pain Inventory Question #5 (average pain). Statistical tests including chi-square for categorical variables and Mann-Whitney Wilcoxon test for continuous variables were conducted to assess differences in demographic and clinical characteristics as well as PROs between patients with and without IPR. A multivariate regression analysis was conducted to assess the relationship between IPR and PROs.

Results: 571 patients treated at 10 hospital centers in China were enrolled. 73% were female, the mean (SD) age was 62 (8.32) years. The number of years with OA ranged from less than one year to over 37 years, suggesting a broad sample of patients. Most patients were impacted by knee OA only (90%). Almost half (43%) of the study population met the definition of IPR. Patients with IPR tended to be older, have greater prevalence of obesity, have more comorbidities, and had longer disease duration. The majority (98%) of patients were receiving nonsteroidal anti-inflammatory drugs (NSAIDs), followed by chondroprotective

medications (23%). However, more patients with IPR mentioned being dissatisfied with treatment (38% vs. 21%). After adjusting for covariates, patients with IPR reported worse HRQOL, more functional limitations, and reduced work productivity compared to patients without IPR.

Conclusion: IPR is highly prevalent among individuals with knee and/or hip OA in China and is associated with decreased HRQOL and work productivity, impaired function, and treatment dissatisfaction. Developing awareness among healthcare professionals about the presence and potential impact of IPR is important for the ultimate improvement of OA patient management.

PRO mean (SE)	No IPR (N=328)	IPR (N=243)
EQ-5D Index	0.72 (0.01)	0.49 (0.02)
EQ-5D VAS	72.3 (0.85)	65.5 (1.00)
WOMAC Pain Subscale	13.1 (0.78)	22.7 (1.52)
WOMAC Stiffness Subscale	4.2 (0.27)	7.4 (0.51)
WOMAC Physical Function Subscale	44.8 (2.61)	76.9 (5.07)
Work Productivity Loss	30.0 (4.07)	47.5 (10.46)

Multivariate analysis adjusted for age, year since OA diagnosis/follow-up, gender, BMI, number of medication classes, insurance, physician specialty/academic responsibilities, number of affected joints, diabetes, CVD, hyperlipidemia/hypertension, and depression. All differences were statistically significant ($p < 0.05$) except work productivity loss ($p=0.11$)

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FRI0429 UROLITHIN B ATTENUATES THE INFLAMMATORY AND NITROSATIVE STRESS ON INTERLEUKIN-1 INDUCED CHONDROCYTES

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Background: Osteoarthritis (OA) is one of the most common degenerative disorders with cartilage degradation especially to the elderly resulting in disability. Many inflammatory cytokines involve the pathogenesis of the OA and causes destruction and decomposition of articular cartilage, including interleukin 1 beta (IL-1 β). Urolithin B is a small polyphenolic compound, produced by gut flora from ellagitannins-rich foods, such as pomegranate, strawberries, raspberries, etc. Urolithin B has been documented in anti-inflammatory and antioxidant properties. However, the mechanism underlying the effects of Urolithin B on IL-1 stimulated human osteoarthritis (OA) chondrocytes remains unrevealed

Objectives: The aim of this study was to investigate the biologic effects of Urolithin B on OA models and associated mechanism.

Methods: Primary culture of human chondrocyte, knee joint obtained from total knee replacement of patients with osteoarthritis, were used IL-1 β induced and treated with/without 100 μ M Urolithin B for 24 hours respectively. Total cell lysates were collected for western blotting to analyze the catabolic molecules. Culture medium were collected for gelatin zymography to analyze the secretion of MMP 2 and 9.

Results: Urolithin B inhibits the overexpression of not only inflammatory marker COX2 and nitrosative marker NOS2, but also matrix metalloproteinases (MMPs)-1, -3, 13 in IL-1 β induced chondrocytes by western blotting. It also restored the IL-1 β induced glycosaminoglycan degeneration in ex vivo articular cartilage evaluated by Safranin O stain. Meanwhile, Urolithin B can activate autophagy, increasing LC3 II/I ratio, in IL-1 β induced chondrocytes.

Conclusion: Collectively, the study demonstrates that Urolithin B may be of value in the treatment of osteoarthritis through its anti-inflammatory, anti-oxidant and anti-proteinase activities.

References:

- [1] Decker, R.S., E. Koyama, and M. Pacifici, *Articular Cartilage: Structural and Developmental Intricacies and Questions*. Curr Osteoporos Rep, 2015. 13(6): p. 407-14.

- [2] Luo, Y., et al., *The minor collagens in articular cartilage*. Protein Cell, 2017. 8(8): p. 560-572.
- [3] Sophia Fox, A.J., A. Bedi, and S.A. Rodeo, *The basic science of articular cartilage: structure, composition, and function*. Sports Health, 2009. 1(6): p. 461-8.
- [4] Carballo, C.B., et al., *Basic Science of Articular Cartilage*. Clin Sports Med, 2017. 36(3): p. 413-425.
- [5] Taruc-Uy, R.L. and S.A. Lynch, *Diagnosis and treatment of osteoarthritis*. Prim Care, 2013. 40(4): p. 821-36, vii.
- [6] Rhon, D., Re: Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008;16:137-62. Osteoarthritis Cartilage, 2008. 16(12): p. 1585; author reply 1589.
- [7] Wang, S.T., et al., Antimelanogenic Effect of Urolithin A and Urolithin B, the Colonic Metabolites of Ellagic Acid, in B16 Melanoma Cells. J Agric Food Chem, 2017. 65(32): p. 6870-6876.

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Title:

Urolithin B attenuates the inflammatory and nitrosative stress on interleukin-1 induced chondrocytes

Key words: Urolithin B, Osteoarthritis, chondrocytes, Cyclooxygenase 2, Nitric Oxide Synthase 2, matrix metalloproteinase

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FRI0430 THE NOVEL, INTRA-ARTICULAR CLK/DYRK1A INHIBITOR LORECEVIVINT (LOR; SM04690), WHICH MODULATES THE WNT PATHWAY, IMPROVED RESPONDER OUTCOMES IN SUBJECTS WITH KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS FROM A PHASE 2B TRIAL

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Background: Lorecivint (LOR; SM04690) is a small-molecule, intra-articular (IA) CLK/DYRK1A inhibitor that modulates the Wnt pathway¹ and has demonstrated some beneficial effects on patient-reported outcomes (PROs) relative to placebo (PBO) in two Phase 2 knee OA trials. With subjective measures such as PROs, meaningful benefits may be better characterized by representation as discrete threshold responses rather than by changes in mean point estimates.

Objectives: To conduct a post hoc analysis of subjects in a 24-week Phase 2b study by measuring the proportions of subjects treated with LOR and placebo (PBO) who achieved 30%, 50%, or 70% threshold responses of improvement over baseline in Pain Numeric Rating Scale (NRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and Patient Global Assessment (PtGA) at Week 12. Results from the Phase 3-selected dose of 0.07mg LOR are presented here.

Methods: Subjects had ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2–3, and Pain NRS scores ≥ 4 and ≤ 8 in the target knee and < 4 in the contralateral knee. A single 2mL IA injection of 0.03mg, 0.07mg, 0.15mg, or 0.23mg LOR, or vehicle PBO was given in the target knee at baseline. The proportion of subjects meeting 30%, 50%, or 70% threshold responses over baseline in the weekly average of daily Pain NRS [0–10], WOMAC Pain [0–100], WOMAC Function [0–100], and PtGA [0–100] at Week 12 was determined. The odds ratios (OR [95% CI]) of achieving each threshold response level were calculated and compared between LOR and PBO.

Results: In total, 635 subjects (91.4%) completed the study (mean age 59.0 $\pm$ 8.5 years, BMI 29.0 $\pm$ 4.0 kg/m², female 58.4%, KL grade 3 57.3%). At Week 12, treatment with 0.07mg LOR significantly ($P < 0.05$) increased the odds of a 30% threshold response in Pain NRS (OR 2.47 [1.45, 4.19]) and WOMAC Function (OR 1.86 [1.10, 3.12]) and a 50% threshold response in WOMAC Pain (OR 1.79 [1.06, 3.03]) and PtGA (OR 2.28 [1.25, 4.16]). Numerically, more (not statistically significant) subjects achieved a 70% threshold response in all PROs. All improvements were maintained through Week 24.