Figure 1 Cost-effectiveness plane for the comparison of implementation of a structured model for OA care (intervention group) and usual care (control group)

Conclusion: The results of the cost-utility analysis show that implementing a structured model for OA care in primary healthcare based on international guidelines is highly likely a cost-effective alternative compared to usual care for people with hip and knee OA. More studies are needed to confirm this finding, but this study results indicate that implementing structured OA care models in primary healthcare may be beneficial for the individual as well as for the society.

Disclosure of Interests: None declared

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Emerging molecular targets in OA

OP0199

EX VIVO BIOMARKER PROFILING IDENTIFIES ONCOSTATIN-M AS SPINE OSTEOARTHRITIS-SPECIFIC OSTEOIMMUNOLOGICAL TARGET

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Background: Disease heterogeneity, both clinically and molecularly, has been a major hurdle in the development of efficacious disease-modifying osteoarthritis drugs (DMOADs). Biomechanical, inflammatory, osteoporotic and metabolic OA have been proposed as clinically relevant subtypes for stratification of knee OA patients, yet this remains to be included in clinical trial design. Disease heterogeneity does not only occur within, but also between joint types. However, robust data on joint-specific pathomechanisms of OA are still lacking.

Objectives: In this study, we performed ex vivo biomarker profiling of human osteochondral tissue of knee and spine OA to identify joint-specific pathomechanisms and DMOAD treatment responses.

Methods: Facet joint and tibial plateaus were obtained from patients undergoing lumbar spinal fusion (n=11, mean age 72.8) and total joint arthroplasty (n=8, mean age 73.0) respectively. Osteochondral specimens were cut in equal-sized samples (100-300 mg wet weight) and randomly assigned to treatment groups: control (DMSO), inflammation (1 µg/mL LPS) or inflammation + DMOAD (TGF-beta type I receptor inhibitor, 10 µM SB-505124). Explant culture was conducted for one week and biomarkers of bone metabolism (Pro-Col-1a, SOST, OPG, SPP1), inflammation (MCP-1, IL-6, MMP3, OSM, TIMP1, VEGFA) and cartilage metabolism (ACAN, COMP) were determined by ELISA. Normalized biomarker secretion was analysed using clusteranalyses and ANOVA. Cartilage proteoglycans were assessed by whole mount Alcian blue staining. Expression of Oncostatin-M (OSM) and its receptors OSMR and LIFR in joint tissues was assessed by RT-PCR and immunohistochemistry.

Results: Clusteranalyses revealed that LPS stimulation increased IL-6 and MCP-1 secretion by both facet joint (FJ) and knee joint (KJ) tissues. Interestingly, Oncostatin-M (OSM) and its downstream mediators MMP3 and TIMP1 were increased in the majority of FJ, but not KJ specimens. Statistical analyses corroborated increased OSM, MMP3 and TIMP1 levels in a spine-specific fashion (Figure).

Whole mount Alcian blue staining revealed heterogeneous effects of LPS treatment on cartilage proteoglycans, which was negatively correlated with OSM ($r=-0.54$) and TIMP1 levels ($r=-0.45$) – yet poorly associated with ACAN ($r=0.19$). Inhibition of TGF-beta type I receptor signalling in osteochondral tissues led to a drastic reduction of Pro-Collagen-1a and IL-6 secretion in both spine and knee OA specimens. Interestingly, DMOAD treatment significantly reduced OSM, TIMP1 and MMP3 levels in FJ specimens only. Vice versa, KJ tissues revealed a specific upregulation of monocyte chemoattractant protein-1 (MCP-1) and osteopontin (SPP1) upon inhibition of TGF-beta signalling. OSM was exclusively expressed in subchondral bone marrow macrophages. Isolated chondrocytes and osteoblasts expressed both LIFR and OSMR, yet intact cartilage only showed OSMR expression, while OSMR and LIFR was expressed in marrow tissue

Conclusion: Oncostatin-M expression and signalling was uncovered as specific pathomechanism of spine OA. DMOAD treatment effects suggested interplay of OSM and TGF-beta signalling pathways in facet joint osteoarthritis. Known to be predominantly expressed by macrophages and immune cells, OSM may be an important osteoimmunological mediator of tissue damage and remodelling in spine, but not knee OA. This study also highlights the value of ex vivo human tissue models for OA phenotyping and preclinical evaluation of DMOADs.

Disclosure of Interests: None declared

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OP0200

BLOCKING ROR2 IMPROVES CARTILAGE INTEGRITY AND PROVIDES PAIN RELIEF IN OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is the leading cause of chronic disability worldwide, affecting 12% of the population, and yet we still do not have a disease-modifying treatment. Cartilage breakdown is the hallmark of OA, and patients suffer from pain and loss of joint function/independence, severely affecting quality of life. Therefore, there is a huge unmet clinical need.

Receptor tyrosine kinase-like orphan receptor 2 (ROR2) is a non-canonical WNT receptor that regulates the planar cell polarity pathway, controlling limb outgrowth during development. During skeletal development, chondrocytes require ROR2 to undergo hypertrophy throughout the process of endochondral bone formation¹. Loss of function mutations in humans causes Recessive Robinow Syndrome, leading to limb shortening and brachydactyly^{2,3}.