in the study. All early RA pts and 4 SLE pts were not treated with glucocorticoids and disease-modifying antirheumatic drugs. Six SLE pts received low-dose glucocorticoids and hydroxychloroquine.

All pts were assessed for macrophage activation and laboratory data: ESR, RF, ACCP, CRP, ANA, anti-dsDNA. Isolation of monocytes was carried out according to the standard procedure for obtaining a leukocyte fraction in a Ficoll gradient and subsequent selection of CD14+ cells using magnetic separation. After isolation, the cells were cultured in X-Vivo medium. To assess the degree of monocyte activation, cells were stimulated by the addition of LPS. The value of monocyte activation was expressed as a ratio of the level of secretion of proinflammatory cytokines by monocytes cultured with and without LPS addition. Secretion levels were determined by ELISA. The belonging of the isolated cells to CD14+ monocytes was additionally confirmed by flow cytometry.

Results: Macrophage activation was 2.6 (2.0;5.4) and 4.8 (2.8;7.3) in RA and SLE pts, respectively ($p>0.05$). In RA and SLE pts macrophage activation was independent of age, sex, body mass index, traditional risk factors (arterial hypertension, overweight, smoking, family history of cardiovascular diseases), RA activity scores (DAS28, SDAI), and SLDAI-2K. No association was found between macrophage activation and levels of ESR, RF, ACCP, CRP, ANA, and anti-dsDNA.

Conclusion: No differences in macrophage activation were found in RA and SLE pts. Macrophage activation was independent of age, sex, traditional risk factors, and ARD-related parameters. A study on a larger number of pts will clarify the link between macrophage activation and autoimmune disorders.

This work was supported by the Russian Science Foundation (Grant № 21-15-00225).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2285

AB0034 PD-1 AGONISM INHIBITS ACTIVATION OF PLASMACYTOID DENDRITIC CELLS

I. Banerjee¹, L. Edwards¹, P. Halvey¹, S. Alioto¹, D. Cluckley¹, C. Mitchell¹, C. Cox¹, E. Lurier¹, M. Cianci¹, S. Bengeri¹, S. Borthakur¹, K. Kis-Toth¹, N. Higginson-Scott¹, J. Viney¹, K. L. Otipoby¹. ¹Pandion Therapeutics, Immunology, Watertown MA, United States of America

Background: T cell function is regulated by complex signaling networks of interconnected activators and inhibitors. Blockade of inhibitory receptors such as programmed death-1 (PD-1) has emerged as a novel treatment for multiple forms of cancer. One of the most common adverse events associated with blockade of the endogenous PD-1/PD-L1 pathway is the induction of autoimmune pathology in multiple tissues, demonstrating that PD-1 activation is necessary for normal immune homeostasis in humans (Kostine, et al., 2018). Given this body of clinical data, we sought to develop a PD-1 agonist antibody as a therapeutic approach to restore immune homeostasis in patients living with autoimmune diseases. PD-1 expression and function has been primarily described on T cells (Ishida, et al., 1992), with additional data available from several other immune cell populations (Ohaegbulam, et al., 2015).

Objectives: To study the effect of PD-1 agonism on plasmacytoid dendritic cell (pDC) function.

Methods: Human PBMCs stimulated with or without toll-like receptor (TLR)-9 agonist, CpG were analyzed by flow cytometry for PD-1 expression on immune cell subsets. To assess the impact of PD-1 agonist on pDC function human PBMCs were activated by CpG in the presence or absence of PD-1 agonist. Type-I interferon (IFN) levels were quantified using ELISA from culture supernatants. The expression of interferon stimulated genes was analyzed by qPCR as a measure of type-I IFN activation.

Results: We have discovered that TLR9 activation can induce PD-1 expression on plasmacytoid dendritic cells, which has not been previously reported. Further, we have demonstrated that PD-1 agonism inhibits TLR9-mediated activation and the effector functions of plasmacytoid dendritic cells.

Conclusion: These data suggest the potential of PD-1 as a target for regulating diseases with pathology generated by type-I IFN.

REFERENCES:

- [1] Ishida, Y., Agata, Y., Shihabihara, K., & Honjo, T. (1992). Induced expression of PD-1, a novel member of the immunoglobulin gene superfamily, upon programmed cell death. *EMBO J.*, 11(11):3887-95.
- [2] Kostine, M., Rouxel, L., Barnetche, T., Veillon, R., Martin, F., Dutriaux, C., ... Schaefferbeke, T. (2018). Rheumatic disorders associated with immune checkpoint inhibitors in patients with cancer-clinical aspects and relationship with tumour response: a single-centre prospective cohort study. *Annual Rheumatic Disease*, 77(3):393-398.
- [3] Ohaegbulam, K. C., Assal, A., Lazar-Molnar, E., Yao, Y., & Zang, X. (2015). Human cancer immunotherapy with antibodies to the PD-1 and PD-L1 pathway. *Trends in Molecular Medicine*, 21(1); 24-33.

Disclosure of Interests: Ishita Banerjee Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Lindsay Edwards Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Patrick Halvey Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Salvatore Alioto

Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, David Cluckley Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Caitlin Mitchell Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Christopher Cox Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Emily Lurier Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Michael Cianci Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Soumya Bengeri Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Susmita Borthakur Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Katalin Kis-Toth Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Nathan Higginson-Scott Shareholder of: Pandion Therapeutics, Consultant of: Biotech Companies, Employee of: Pandion Therapeutics, Jo Viney Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics, Kevin L. Otipoby Shareholder of: Pandion Therapeutics, Employee of: Pandion Therapeutics

DOI: 10.1136/annrheumdis-2021-eular.2682

Osteoarthritis, aetiology, pathology and animal models

AB0035 A REVIEW OF THE CLINICAL AND ECONOMIC BURDEN OF OSTEOARTHRITIS PAIN BY SEVERITY IN THE UNITED STATES

A. Sadosky¹, P. Schepman², S. Thakkar², R. Robinson³, C. Beck⁴. ¹Apperture LLC, HEOR, Westley, United States of America; ²Pfizer Inc, PHU, New York, United States of America; ³Eli Lilly and Company, Global Patient Outcomes & Real World Evidence, Indianapolis, United States of America; ⁴Pfizer Inc, Medical Affairs, Tadworth, United Kingdom

Background: The development of new therapies to treat symptomatic osteoarthritis (OA) often requires targeting patient subgroups such as mild and/or moderate and/or severe. Multiple assessments for pain are used in clinical and research settings, yet to quantify patient burden with increasing pain severity it is important to understand the potential variability in outcomes based on definitions of severity used¹.

Objectives: The objective of this study was to examine studies in the published literature that report the burden of OA pain by severity to assess similarities and/or differences across study methodologies and outcomes.

Methods: A targeted literature review of PubMed and Google Scholar was conducted January 2021 and included search terms: osteoarthritis, severity, United States (US), burden, quality of life, medication/treatment, and healthcare resource utilization. The search was limited to the English language, full-text articles, and no restriction on publication date. Results included a recent study of the burden of symptomatic OA pain respondents by severity level in the US^{2,3}. Over 100 publication titles were reviewed. Comparison of findings was descriptive in nature.

Results: Nine publications were identified representing 7 unique studies, 6 being patient and/or healthcare provider surveys. Two studies focused on OA severity: the remaining 5 stratified patients by pain severity, and all but 2 of the 5 identified and confirmed pain as OA-related. Pain measures included numeric rating scales (generic 0-10, Western Ontario and McMaster Universities Arthritis Index [WOMAC] NRS 3.1), visual analog scales (generic 0-100, Short-Form McGill Pain Questionnaire Visual Analog Scale [SF-MPQ-VAS]) or Pain Interference with Activities (PIA) scale derived from the 12-Item Short Form Health Survey [SF-12v2] developed for the Medical Outcomes Study, with recall periods varying from 48 hours to 7 days to 4 weeks. Only one study exclusively assessed symptomatic patients only i.e., patients with pain scores of 0 were excluded; the remainder compared cohorts of no/mild pain with increasing severity cohorts. Four of the 7 studies examined pairwise differences among mild, moderate, and severe patients (1 study vs. a non-OA cohort); 2 compared no/mild vs. moderate-to-severe OA pain and 1 study compared mild to moderate-to-severe OA pain. For most outcomes examined like clinical comorbidities, quality of life, and healthcare resource utilization, increasing burden was observed with increasing OA and/or pain severity despite study variability.

Conclusion: Pain severity levels represent an important and distinguishing factor that contributes to health outcomes in OA patients in the US. Considerable heterogeneity across studies may impact how OA pain is defined, perceived by patients, and treated. Selecting appropriate OA pain severity assessments, including cut-points, may contribute to the successful monitoring of outcomes or comparisons of therapies to manage symptomatic OA pain, especially those that target specific pain severity subgroups.

REFERENCES:

- [1] Hawker GA, Mian S, Kendzerska T et al. Arthritis Care and Research. 2011; 63(11):S240-S252.
- [2] Schepman P, Robinson RL, Thakkar S, et al. International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Virtual Annual Meeting; May 2020.
- [3] Schepman P, Thakkar S, Robinson RL, et al. PAINWeek 2020 Virtual Meeting; September 2020.

Disclosure of Interests: Alesia Sadosky Shareholder of: Own stock in Pfizer Inc, Consultant of: I am an employee with the consulting firm Apperture Health, Employee of: I am retired from Pfizer Inc, Patricia Schepman Shareholder of: Owns shares in Pfizer Inc, Employee of: Employee of Pfizer Inc, Sheena Thakkar Shareholder of: Owns shares of Pfizer Inc, Employee of: Employee of Pfizer Inc, Rebecca Robinson Shareholder of: Owns shares of Eli Lilly and Company, Employee of: Employee of Eli Lilly and Company, Craig Beck Shareholder of: Owns shares of Pfizer Inc, Employee of: Employee of Pfizer Inc
DOI: 10.1136/annrheumdis-2021-eular.534

AB0036

APPA (APOCYNIN AND PAEONOL) REDUCES ROS PRODUCTION AND SENESENCE IN HUMAN ARTICULAR CHONDROCYTES

M. Fernandez-Moreno¹, N. Larkins², A. Reynolds², T. Hermida Gómez^{1,3}, F. J. Blanco¹. ¹ Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). CICA-INIBIC., Servicio de Reumatología., A Coruña, Spain; ²AKL Research & Development, Stevenage Bioscience, Stevenage SG1 2FX., United Kingdom; ³Centro de Investigación Biomédica en Red, Bioingeniería, Biomateriale y Nanomedicina, (CIBER-BBN), Madrid, Spain

Background: Disease modification is not yet possible for osteoarthritis (OA). Mitochondrial ROS and pro-inflammatory cytokines are involved in the pathogenesis of OA and are potential therapeutic targets. APPA, a combination of apocynin (AP) and paeonol (PA), has the potential capacity to modulate synthesis of pro-inflammatory stimuli.

Objectives: To investigate the anti-inflammatory effect of APPA in human articular chondrocytes and cartilage.

Methods: Tissue and chondrocytes from human OA cartilage were isolated. The effect of APPA on chondrocyte viability was analyzed using MTT. IL-1 β 10 ng/mL and LPS 10 ng/mL were used as pro-inflammatory stimuli. ROS production was evaluated by flow cytometry using DCFH-DA and MitoSoxRed. The percentage of senescent cells was evaluated through the quantification of Fluorescein di- β -D-galactopyranoside (FDG) by flow cytometry. The effect of APPA on gene expression of pro-inflammatory cytokines (IL-8 and TNF- α) and enzymes degrading cartilage (MMP-13 and MMP-3) were analyzed in chondrocyte and cartilage by RT-PCR. Quantification of Toluidine Blue (TB) staining in cartilage was performed to evaluate proteoglycans content using software ImageJ/Fiji. Release of Glycosaminoglycan (GAGs) into the supernatant was quantified using BlyscanTM Glycosaminoglycan assay. Statistical analyses were performed with GraphPad Prism v6.

Results: Chondrocytes, incubated in presence of APPA 10 μ g/mL for 24 h had viability >85%, reduced cytoplasmic ROS (p=0.028) and mitochondrial anion superoxide production induced by LPS 10 ng/mL (p=0.057). Chondrocytes incubated in presence of APPA 10 μ g/mL for 2 hours contained significantly fewer senescent cells (p=0.0079). APPA significantly reduced the gene expression induced by IL-1 β 10 ng/mL in chondrocytes of IL-8, TNF- α , MMP-13 and MMP-3. Cartilage incubated with APPA 60 and 100 μ g/mL for 48 h showed decreased the MMP-3 gene expression induced by IL-1 β (p=0.021 and p<0.0001 respectively). Quantification of TB showed that APPA 60 and 100 μ g/mL during 48h increased the proteoglycans in intermedial layer, which had been decreased through the incubation with IL-1 β (p=0.0018 and p=0.018 respectively). Quantification of release GAGs into the supernatant decreased significantly when the cartilage explants were incubated for 48h in presence of APPA 100 μ g/mL (p=0.028).

Conclusion: APPA has a clear anti-inflammatory effect on human articular chondrocytes, and could reduce extracellular matrix degradation of cartilage. This could be mediated by the capacity to modulate ROS production and reduce senescence.

Disclosure of Interests: Mercedes Fernandez-Moreno: None declared, Nicholas Larkins Shareholder of: I am a shareholder in AKL Research and Development Ltd, Alan Reynolds Shareholder of: I have share options in AKL Research and Development Ltd, Speakers bureau: I have not been a paid speaker for a pharma company - at least not since 2008 which I think is outside the scope of this, Consultant of: The last time I was a paid consultant was in 2017 when I acted as a consultant for Avillion and Norgine, Employee of: I am also an employee of AKL Research and Development Ltd, Tamara Hermida Gómez: None declared, Francisco J. Blanco Speakers bureau: Lilly Pfizer Sanofi Galapagos, Consultant of: Lilly Pfizer Sanofi Galapagos, Grant/research support from: Lilly MSD Merck Serono Pfizer Pierre-Fabre Roche

Sanofi
Servier
UCB
Abbvie
Amgen
Bioiberica
Bristol Mayer
Celgene
Celltrion
Cellerix
Grunenthal
Gebro Pharma
AKL Research and Development Ltd
DOI: 10.1136/annrheumdis-2021-eular.2027

AB0037

UNDIFFERENTIATED ARTHRITIS

O. Jomaa¹, J. Mahboub¹, S. Zrour¹, I. Bejjia¹, M. Touzi¹, N. Bergaoui¹.
¹University Hospital Fattouma Bourguiba Monastir, TUNISIA, Rheumatology Department, Monastir, Tunisia

Background: Early recognition and treatment of inflammatory arthritis is imperative for the further course of the disease.

Objectives: This study aims to determine the evolution of undifferentiated arthritis observed in rheumatology.

Methods: Retrospective descriptive study which collects patients files identified as undifferentiated Arthritis and followed in the Rheumatology Department at Fattouma Bourguiba Hospital Monastir TUNISIA over a period of 15 years (2005, 2019). Epidemiological, clinical, paraclinical, and evolutionary data were collected and analyzed.

Results: 99 files were analyzed. The average age was 42.06 $\pm$ 15.56; they were 42 males and 57 females with an average body mass index of 27 $\pm$ 6.1 Kg/m². The reason leading to consultation was, polyarthritis (37), oligoarthritis (27), mono-arthritis (21), and polyarthralgia (15). The median time to visit was 60 days [15 days, 3 months]. The median number of painful joints and swollen joints was 4 [2, 8], and 2 [1, 4] respectively. The mean duration of morning derusting was 34.8 $\pm$ 24.4 minutes. Extra-articular manifestations were: a dry syndrome (22), a rheumatoid nodule (2), and serosal damage (1). Anemia (52 patients), leukopenia (6 patients), and lymphopenia (13 patients) were found in the blood cell count with a biological inflammatory syndrome in most patients (72/99). The immunology results showed: positive anti-nuclear antibodies (15/99), positive Anti-Citrullinated Protein Antibodies (9/99) and positive rheumatoid factor (8/99). 31 patients had standard radiological signs represented mainly by joint pinching and erosions. A joint puncture was done in 36/99 revealing inflammatory fluid in most cases. After an average follow-up of 1047 days [365, 1460]. undifferentiated arthritis was classified as rheumatoid arthritis (RA) (23), spondyloarthritis (SpA) (10), connective tissue disease (11), Crystalline Arthritis (5), and paraneoplastic arthritis (2). One patient had self resolution of symptoms and 38 remain undifferentiated. we found that the more the patients were seropositive, the more likely to develop Rheumatoid Arthritis (p=0.001), the more there was disorder in the blood cell count, the more the evolution was towards connective tissue disease (0.01), The more male patients were, the more likely to develop SpA (p=0.04). The patients management was mainly based on: analgesics (94), systemic corticosteroids (57) with a mean dose of 10.89 $\pm$ 5.8 mg/day. The use of Methotrexate and antimalarial drugs was noted in 18 and 15 patients respectively.

Conclusion: Follow-up of patients with undifferentiated arthritis leads to a definite inflammatory rheumatism diagnosis in 61.6% of cases. Our data indicate that seropositive patients with chronic symptoms carry an increased risk of developing Rheumatoid Arthritis (P=0.001). Clinical, biological and genetic data can help the health care provider to predict future outcomes.

REFERENCES:

[1] DOI: 10.1007/s00132-018-3539-2.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2309

AB0038

CIRCULATING MICRORNAS IN HAND OSTEOARTHRITIS

A. Pekacova^{1,2}, J. Baloun¹, O. Sleglova^{1,2}, O. Růžicková^{1,2}, J. Vencovsky^{1,2}, K. Pavelka^{1,2}, L. Šenolt^{1,2}. ¹Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic; ²First Faculty of Medicine Charles University, Department of Rheumatology, Prague, Czech Republic

Background: microRNAs (miRNAs) are small non-coding RNAs that can ignite the degradation of mRNAs or inhibit the protein translation and are therefore essential for several physiological and pathological functions. miRNAs can regulate up to 60 % of human mRNA, including genes related to cartilage development, homeostasis, and OA pathology. For example, miR-9 inhibits matrix metalloproteinase 13