Results: 10,145 RA patients were identified who used index drugs from the database (mean age 57 years, 82% female). Among them, 6,986 patients had identifiable dates for RA diagnosis (mean age 57 years, 79% female). The mean (SD) duration from RA diagnosis to index drug initiation was 1,425 (1,162) days with 1,509 (22%) patients having a duration ≤ 1 year. At diagnosis, the most common 1st cDMARD used was hydroxychloroquine (63%), followed by MTX (55%) and sulfasalazine (29%) with steroids used in 75%. During the 1 year from the diagnosis, 85% of patients eventually used MTX, 42% ever used MTX ≥ 15 mg/week, only 3% used parenteral MTX, and 85% patients used combined cDMARDs with a mean 188 days from the RA diagnosis to combination therapy. Patients whose maximal MTX dose reached 20mg/week were rare (9%) and 62% were still on steroid after 1 year.

During the 1 year prior to the index drug use ($n = 10,145$), the most common cDMARD was MTX used in 89% patients with 46% who ever used ≥ 15 mg/week and 4% of parenteral users, followed by hydroxychloroquine (55%), leflunomide (52%), sulfasalazine (38%), and tacrolimus (20%). All patients used combination therapy and 98% steroids.

Conclusion: These data indicate that a substantial proportion of RA patient did not try maximal dose or parenteral use of MTX during the 1 year post-diagnosis as recommended by the current treatment guideline. Instead, they often used cDMARDs combination therapy. During the 1 year before initiating bDMARDs or JAKis, they were treated with intensive cDMARD combination therapy rather than escalating their MTX dose.

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THU0178

THE EFFECT OF TOLEROGENIC DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SMALL PILOT TRIAL

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through the presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, utilization of tolerogenic DCs seems to be a promising immunotherapeutic tool to treat RA.

Objectives: The aim of our study is to evaluate the safety and tolerability of a single intra-articular injection (into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN- α /GM-CSF and tolerized with Dexamethasone in RA patients.

Methods: DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN- α in the presence dexamethasone, applied on third day. Azoximer bromides maturation stimuli was added on fourth day. Twelve RA patients with moderate and high disease activity and ultrasound-defined kneesynovitis were recruited in this study. All patients fulfilled ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. The patients received intra-articular injections of 1×10^6 , 3×10^6 , 5×10^6 , 8×10^6 , 10×10^6 DCs in knee joints. Safety was assessed by evaluation of adverse events (AE). Acceptability was assessed by questionnaire. DAS28 and HAQ were used for assessment of treatment efficiency. This trial registered on clinicaltrials.gov (ID: NCT03337165).

Results: DCs injections were safe and well tolerated. No one participants showed worsening of symptoms in targeting knee, fever, elevation of blood pressure or other AE within 7 days after injection. All patients,

evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR > 1.2). The median DAS28-ESR decreased from 5.1 to 3.1 ($p=0.03$). The median pain VAS score decreased from 52 (41-70) mm to 42 (15-55) mm; $p=0.04$. In addition, we detected median HAQ improvement (from 1.45 to 1.0; $p=0.04$). The effect of treatment had been continued for 6 months and after that we indicated escape of effect.

Conclusion: The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and have a potential not long term efficiency and requires the repeating of procedure.

Disclosure of Interests: None declared

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THU0179

PATIENT AND THEIR ILLNESS – ATYPICAL SOURCES OF THERAPY RISKS. CHARACTERISTICS OF THE USE OF METHOTREXATE (MTX) AND FOLIC ACID (FA) SUPPLEMENTATION IN THERAPY LASTING MINIMUM 8 WEEKS IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: MTX is a well-established treatment with an anchor role in RA (1). Patients being treated for RA must pay attention to the specific dosage of drugs and the different routes of administration. Additionally they suffer from the inconvenience related to the progression of the disease.

Objectives: We observed patients diagnosed with RA, who were treated with subcutaneous (SC) MTX and possible risks associated with this therapy. The attention paid to the inconvenience for the patient associated with SC form of drug administration and the principles of MTX dosing with FA supplementation.

Methods: 32 rheumatologists were invited to non-interventional, post marketing observation. They collected information from 690 patients who already received a minimum of 1 dose of MTX SC. As part of a standard medical visit, the sociographic data of the patient and information obtained during the medical interview as well as subjective and objective examination were recorded in the prepared form. Data was collected on a weekly basis over a period of 8 weeks. The protocol was compliant with the regulatory and ethical requirements in the country.

Results: Out of 682 enrolled patients, 581 (85.2%) were sero-positive and 95 (14%) were sero-negative. The average level of anti-CCP antibodies before enrollment was 85.76 Units. The mean time from the diagnosis of the underlying disease was 28.7 months. The vast majority of patients confirmed that they had previously used FA supplementation (92.2%), only 10 patients showed DAS28 at the remission level. During each visit no adverse events (AE) were reported in over 90% of patients. The most commonly reported AE are nausea or weakness. No severe, life threatening AE were recorded.

Patients evaluated the pain of the injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Most patients assessed the pain of injections as the minimum (1) (56.5% - week 1 (W1), 52.9% - W2, 56.7% - W3, 61.5% - W4, 56.7% - W5, 53.8% - W6, 65.2% - W7, 61.8% - W8). The second most frequently mentioned pain assessment by respondents was 2 (34.6% - W1, 35.3% - W2, 34.3% - W3, 29.2% - W4, 34.3% - W5, 38.5% - W6, 26.1% - W7, 32.9% - W8). No patients reported values between 6 and 10. Patients also assessed how the pain at the site of injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Each week, more than half of the patients assessed pain at the injection site as 1 (55.9% - W1, 56.7% - W2, 56.7% - W3, 57.8% - W4, 50.8% - W5, 62.5% - W6, 60.3% - W7, 61.6% - W8). Patients did not report any value of 5-10. More than seven out of ten patients reported FA administration the day 2 of their therapy (76.5%, at W1). In remaining days FA supportive therapy reported 30.3-52.3% of patients (2).

Conclusion: Neither pain related with injection nor local AE was reported as a significant issue by patients. Adherence to FA administration recommendation is low. This should be evaluated in further studies, but there is a risk that inappropriate FA administration may reduce efficacy of MTX treatment.

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Disclosure of Interests: Piotr Ligocki Consultant for: Accord Healthcare, Grzegorz Orlik Employee of: Accord Healthcare, Vishal Vekariya Employee of: Intas Pharmaceuticals
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THU0180

INFLUENCE OF BLUE MUSSEL (MYTILUS EDULIS) INTAKE ON FATTY ACID COMPOSITION IN ERYTHROCYTES AND PLASMA PHOSPHOLIPIDS AND SERUM METABOLITES IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: The positive effects of omega-3 on risk of cardiovascular disease, on inflammation and immune function are well established [1]. Unfortunately fish as a source of omega-3 is not economically or environmentally sustainable. In contrast, blue mussel farming is beneficial for the environment since excessive nitrogen is removed at harvest and eutrophication of the sea is reduced [2]. Blue mussels contain not only omega-3, but are rich in nutrients such as zinc, selenium, riboflavin and carotenoids. We have previously shown, in the randomized cross-over trial Mussels, Inflammation and RA (MIRA), that disease activity (DAS28-CRP), fatigue, pain and general health in RA is improved by a dietary intervention with blue mussels compared to control [3]. It is not clear what the mechanisms of the intervention were, and if the intake of omega-3 from the blue mussels plays a role.

Objectives: The aim of this study was to investigate if the intake of blue mussels in patients with RA lead to changes in fatty acid composition in plasma phospholipids and erythrocytes and/or in metabolites (detected by NMR-metabolomics), compared to a control diet, in an attempt to understand the health beneficial effects found in the MIRA study.

Methods: Twenty-three women completed the randomized 2 × 11-week cross-over dietary intervention, exchanging one cooked meal a day, five days a week, with a meal including 75 g blue mussels or 75 g meat. Fatty acid composition in erythrocytes and plasma and ¹H-NMR metabolomics data were analysed and multivariate data analysis; Orthogonal Projections to Latent Structures with Discriminant Analysis (OPLS-DA) and OPLS with effect projections (OPLS-EP) were performed to compare the two diets.

Results: Intake of the blue mussels led to a different fatty acid profile in erythrocytes, compared to control, and all samples could be correctly classified with OPLS-DA (figure 1). The changes included significant increases in omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The patterns for plasma phospholipids and ¹H-NMR serum metabolites were not as specific for the diets and metabolites were strongly influenced by body mass index (BMI) (figure 2).

Abstract THU0180 – Figure 1. A) Model prediction for all individuals in OPLS-EP models for erythrocyte fatty acids (%). B) OPLS-DA models showing separation for erythrocyte fatty acids (%). Black boxes = control diet, grey circles = blue mussel diet

Abstract THU0180 – Figure 2. Orthogonal Projections to Latent Structures (OPLS) for metabolites in relation to significant related factors (n=92). TAG= triacylglycerides, BML= body mass index

Conclusion: To conclude, the change in fatty acid pattern in erythrocytes could be related to reduction in disease activity in the MIRA-study, although it cannot be excluded that other factors than omega-3 fatty acids potentiate the effect. Multivariate modelling of fatty acids in erythrocytes increased the precision for compliance, compared to evaluating EPA and DHA content alone.

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Disclosure of Interests: Helen Lindqvist Employee of: Yes, for Janssen-Cilag AB in 2001-2003, Before I was a PhD-student and within a different field (dementia). My research field is within diet and Rheumatology., Inger Gjerdtsson: None declared, Philip Calder: None declared, Linnea Barebring: None declared

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THU0181

TREATMENT WITH UPADACITINIB RESULTS IN THE NORMALIZATION OF KEY PATHOBIOLOGIC PATHWAYS IN PATIENTS WITH RHEUMATOID ARTHRITIS: BIOMARKER RESULTS FROM THE PHASE 3 SELECT-NEXT AND SELECT-BEYOND STUDIES

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Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) in the SELECT-NEXT¹ and SELECT-BEYOND² trials, respectively. The pivotal immune regulatory pathway targets served by JAK1 in patients have not been comprehensively explored.

Objectives: To investigate the mode of action (MoA) of UPA in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.

Methods: Patients from the SELECT-NEXT and SELECT-BEYOND (PBO, n=167; UPA 15 mg QD, n=200) studies were randomly selected from the pool of patients with plasma samples available at baseline, Week 2, and Week 12. Samples from 24 age- and sex-matched healthy controls were included. The levels of 92 proteins were analyzed using the Olink[®] Inflammation Panel. Results from both studies were combined. Data were clustered using the Ward (unsupervised) method; correlations were calculated using the Pearson method; and multiple comparisons were corrected using the Benjamini-Hochberg method; all statistical analyses were performed in JMP 13.10 (SAS Institute). Pathway analysis was performed with Ingenuity[®] Pathway Analysis (Qiagen Inc.) version 45868156.