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# Abstracts for the 5th Turkish-Greek Rheumatology Days, October 14-16, 2011, Belek, Antalya

## Oral Presentations

**(OP-101 — OP-407)**

***Selected Abstracts***

### OP-101

#### Hydroxychloroquine changes serum and saliva BAFF levels in patients with primary Sjögren syndrome

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**Background:** B-cell activating factor belonging to the TNF family (BAFF) is considered to play a role in the etiopathogenesis of Sjögren syndrome (SS) by activating B-cells and increasing their life span. Xerostomia is a major symptom of pSS patients and inversely affects patients' oral health related quality of life (oral QoL)

**Objectives:** The purpose of the present study was to evaluate long term changes of BAFF levels in serum and saliva in patients with pSS who were on hydroxychloroquine treatment and determine whether there is an association between oral QoL.

**Methods:** Eleven patients with pSS (mean age:52.0±5.31 years) who were treated with (HQ) at least 2 years, without systemic involvement and oral health problems were selected in the study. Fifteen healthy patients (F/M:10/5 mean age:39.8±7.2 years) with oral infection regarding pericoronitis and irreversible pulpitis as control group were also selected in the study. HQ was withdrawn for 12 weeks. Baseline evaluation was carried out in pSS. Then, HQ treatment was started for 24 weeks. Patients were examined 12 weeks and 24 weeks after HQ treatment. Controls were examined before and a week after dental procedures. Serum and saliva BAFF levels were evaluated with ELISA in patients and controls before and after treatments. Salivary flows of patients and control group were measured. Oral QoL was evaluated by an oral health impact profile-14 (OHIP-14) questionnaire in these examinations.

**Results:** Baseline mean salivary BAFF levels (12.34±7.3 ng/ml) was significantly decreased after 12 and 24 weeks of HQ treatments (3.57±3.29 ng/ml, 0.57±0.61 ng/ml, respectively) (0.005 and p=0.011). Similarly, decrease in serum BAFF levels (4.95±2.95 ng/ml) was observed at 12 and 24 weeks of HQ treatment (2.99±3.09 ng/ml and 0.02±0.05 ng/ml, respectively) (p=0.005 and p=0.012, respectively). Unstimulated salivary flows were similar in patients treated with HQ after 12 weeks (0.52± 0.44 ml/min) and 24 weeks (0.51±0.41 ml/min) (p=0.88) and higher than patients without treatment (0.23±0.18 ml/min) (p=0.005). Moreover, OHIP-14 score (12.45±9.95) were correlated with salivary flow rate 24 after HQ treatment(r=-0.6 p=0.045).

**Conclusion:** Not only salivary and serum BAFF levels were decreased but also improvement in oral health related quality of life was observed in patients with pSS treated with HQ. Disease activity and inflammation can be controlled and salivary flow rate can be increased by using HQ in pSS patients.

## OP-102

### Cellular microRNAs (miRNAs) and Sjögren's syndrome: Candidate regulators of autoimmune response and autoantigen expression

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**Background:** Sjögren's syndrome (SS) is characterized by humoral responses against the Ro/SSA and La/SSB ribonucleoproteins, whereas elevated expression of these autoantigens has been described in the salivary glands (SG) and the SG epithelial cells (SGEC) of SS patients. The mechanisms implicated in the regulation of their expression are not defined. Recently, a novel post-transcriptional regulatory mechanism of gene expression, involving small RNA molecules, called microRNAs (miRNAs), has been identified. Deregulated expression of miRNAs has been implicated in the pathogenesis of autoimmune diseases, including SS. Herein, we sought to investigate the role of miRNAs that are predicted to target Ro/SSA and La/SSB autoantigens in SS. Therefore, we studied their expression in SGECs, peripheral blood mononuclear cells (PBMC) and SG tissues of SS patients and controls and associated their expression with Ro /SSA and La/SSB mRNA expression.

**Methods:** The miRNAs that target the Ro (Ro52/TRIM21 and Ro60/TROVE2) and La mRNAs were predicted by the miRecords database (http://mirecords.biolead.org), which enables the simultaneous analysis by the 11 most recognized miRNA target prediction programs. The expression of both miRNAs and mRNAs was analyzed by real-time PCR in total RNA extracted from SGECs, PBMCs and SG tissues obtained from 11 SS patients and 11 sicca-controls. Non-parametric Mann-Whitney test was employed to analyze statistically significant differences between SS patients and sicca-controls, whereas associations between miRNAs and mRNAs expression were evaluated by non-parametric Spearman's rank correlation analysis.

**Results:** The miRecords computational analysis identified 430, 1258 and 377 miRNAs that target the Ro52/TRIM21, Ro60/TROVE2 and/or La/SSB mRNAs, respectively. To narrow the number, the miRNAS that are predicted to target both Ro (Ro52/TRIM21 and/or Ro60/TROVE2) and La mRNAs, and identified by at least four miRecords-included databases were selected for further investigation. This approach lead to the identification of eleven miRNAs (let-7b, miR-16, miR-129-5p, miR-153, miR-181a, miR-200b, miR-200b*, miR-223, miR-483-5p, miR-573 and miR-583) that target human Ro/SSA and La/SSB mRNAs. miRs 129-5p, 153, 573 and 583 were not expressed in any of the samples studied and miR-200b* was not detected in PBMCs. The miRNAs let-7b, miR-16, miR-181a, miR-200b, miR-200b*, miR-223 and miR-483-5p, were expressed in SGECs, PBMCs and SG tissues. Mann-Whitney analysis revealed that miR-181a in SG tissues, miR-200b in SGECs and miR-223 in PBMCs were significantly upregulated in SS patients compared to sicca-controls (mean±SE: 43.89±18.6 vs 5.525± 1.292, p=0.02, 2426±511.1 vs 965±243.3, p=0.03 and 986200± 503300 vs 50310±13910, p=0.02 in SS vs CT, respectively). Spearman's rank correlation analyses revealed that miR-200b levels was negatively associated with Ro52/TRIM21, Ro60/TROVE2 and La/SSB mRNA expression in SGECs (r=-0.445, p=0.04, r=-0.454, p=0.04 and r=-0.495, p=0.02, respectively). None of the miRNAs examined was found to correlate with Ro52/TRIM21, Ro60/TROVE2 or La/SSB mRNA levels in PBMCs. Finally, the constitutive expression levels of Ro52/TRIM21, Ro60/TROVE2 and La/SSB mRNA molecules by SGECs and PBMCs were similar between SS patients and sicca-controls.

**Conclusions:** Our findings implicate miR-181a, miR-200b and miR-223 in SS, whereas miR-200b role in the regulation of Ro/SSA and La/SSB mRNAs needs particular attention. Further functional studies are needed to shed light in the role of the deregulated miRNAs in disease pathogenesis and autoantigen expression.

## OP-103

### Epitope mapping and reactivity of the autoantigen aquaporin-4

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**Introduction:** Auto-antibobies against the water channel aquaporin-4 (AQP4) are a marker and pathogenetic factor in neuromyelitis optica (NMO), a demyelinating disorder of the central nervous system. Our aim was to identify the B-cell antigenic linear epitopes of AQP4 and investigate similarities with other molecules.

**Methods:** We screened sera from 21 patients positive for anti-AQP4 antibodies, from 47 patients with relapsing-remitting multiple sclerosis (RRMS), from 23 SLE and 23 pSS patients without neurological involvement (disease controls), and from 28 healthy individuals (normal controls). Eleven peptides, spanning the entire intracellular and extracellular domains of the AQP4 molecule, were synthesized and all sera were screened for anti-peptide antibodies by ELISA. Specificity was evaluated by homologous and cross-inhibition assays.

**Results:** NMO-positive sera exhibited reactivity against peptides AQPaa1-22 (42.9% of patients), AQPaa88-113 (33.3%) and AQPaa252-275 (23.8%). All epitopes were intracellular.

Surprisingly, 11% of the RRMS sera reacted with peptide aa252-275. Healthy controls showed no reactivity against the peptides, while disease controls exhibited only non-specific reactivity. A 73% sequence homology was observed between AQPaa257-271, a 15-mer peptide part of peptide AQPaa252-275, and the aa219-233 domain of the Tax1-HTLV-1 binding protein (TAX1BP1), a host (human) protein associated with replication of the HTLV-1 (Human T-Lymphotropic Virus 1). Antibodies against the AQP4 and the TAX1BP1 15-mer peptides were detected in 26.3% and 31.6% of NMO-positive sera respectively. Healthy controls did not react with these peptides. Homologous and cross-inhibition assays confirmed binding specificity.

**Conclusions:** The first B-cell epitope mapping of AQP4 reveals that a significant portion of anti-AQP4 antibodies target linear epitopes, localized in the intracellular domains of the channel. This observation is in agreement with the recent finding of intracellular AQP4 T-cell epitopes. One of the epitopes reacted with sera from RRMS patients. This finding might indicate a common pathogenetic mechanism for demyelination.

## OP-104

### Pro-inflammatory cytokine response to pattern recognition receptor activation of neutrophils and dendritic cells in Behcet's disease

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**Background:** Innate immune response is crucial for the pathogenesis of Behcet's Disease (BD). In this study, inflammasome functions were investigated in dendritic cells (DC) and neutrophils of BD patients through the activation of patern-recognition receptors "RIG-1 like receptors (RLR) and "NOD-like" receptors (NLR).

**Methods:** Active BD patients with mucocutaneous lesions (F/M: 9/7, mean age: 38±13 years) and 17 healthy controls (F/M: 5/12, mean age: 35±8 years) were included in the study. Peripheral blood mononuclear cells and neutrophils were isolated and dendritic cells (DC) were cultured. DCs and neutrophils were activated with RLR ve NLR ligands. Caspase-1 activation was investigated with flow cytometry using 'FLICA Caspase 1 Detection Kit'. IL-1β, IL-6, TNF-α, IFN-α and IL-18 were measured with ELISA, intra-cellular p38 and RIP2 with flow cytometry.

**Results:** IL-1β, TNF-α, IL-6 and IFN-α levels were similarly present in the supernatants of NOD1/2 and RIG2-activated DC cultures compared to HC. Only IL-18 levels were significantly lower after NOD2 activation (BD: 18 pg/ml vs HC: 46 pg/ml, p=0.017), similarly p38 and RIP2 expressions were lower in BD (p38: BD: %1.3 vs HC: %1.8 and RIP2: BH: %1.1 vs SK: %1.9, p=0.037 and p=0.018, respectively). On neutrophils, IL-6 levels were also lower with all ligands [NOD1: BD: 4.4 vs HC: 7.7 pg/ml, p=0.004; NOD2: BD: 3.7 vs HC: 7.8 pg/ml, p=0.006; RIG1: BD: 3.8 vs HC: 8 pg/ml, p=0.004], compared to controls. Similarly, NOD2 activation caused a lower IFN-· secretion in BD neutrophils [BD: 2.5 vs HC: 4.1 IU/ml, p<0.03].

**Conclusion:** In Behcet's disease, inflammasome seems functional in DCs after NOD1/NOD2 and RIG-1 activations for the secretion of pro-inflammatory cytokines IL-1β, TNF-α, IL-6 and IFN-α. This observation suggests that caspase-1 independent pathways may be more prominent in BD pathogenesis.

**Table (OP-104):** Dendritic cell and neutrophil responses in Behcet's disease

| | Behcet's Disease | | | | | | Healthy Controls | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dendritic Cells | | | Neutrophils | | | Dendritic Cells | | | Neutrophils | | |
| | NOD1 | NOD2 | RIG1 | NOD1 | NOD2 | RIG1 | NOD1 | NOD2 | RIG1 | NOD1 | NOD2 | RIG1 |
| Caspase-1 activation (%) | 1.9 | 1.5 | 1.5 | 4.8 | 4.2 | 4.2 | 1.5 | 1.7 | 1.7 | 6.7 | 5.9 | 4.9 |
| P38 (%) | 1.3 | 1.3* | 1.5 | 1.4 | 1.6 | 1.4 | 1.7 | 1.8 | 1.7 | 1.3 | 1.9 | 1.6 |
| RIP2 (%) | 1.1 | 1.1* | 1.1 | 1.5 | 1.1 | 1.2 | 1.7 | 1.9 | 1.4 | 1.8 | 1.7 | 1.7 |
| IL-1, (pg/ml) | 252 | 254 | 198 | 4.5 | 3.8 | 3.6 | 245 | 243 | 149 | 3.6 | 3 | 3.4 |
| IL-18 (pg/ml) | 46 | 18* | 35 | 35 | 46 | 51 | 41 | 46 | 68 | 35 | 29 | 73 |
| IL6 (pg/ml) | 5.6 | 7.7 | 5.6 | 4.4** | 3.7** | 3.8** | 6.7 | 5.4 | 6.2 | 7.7 | 7.8 | 8 |
| TNF-α (pg/ml) | 7.8 | 11 | 7.5 | 9.5 | 7.5 | 8.5 | 13 | 10 | 12 | 11 | 10 | 11 |
| IFN-α (IU/ml) | 1.8 | 2.2 | 2 | 3.2 | 2.5* | 2.9 | 2.2 | 1.6 | 2 | 4.7 | 4.1 | 4.7 |

*p<0.05. **p<0.01

## OP-105

### Micro-RNA analysis reveals novel biomarkers for disease activity and genes implicated in SLE pathogenesis

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**Background:** MicroRNAs (miRNAs) are potent negative regulators of gene expression that have the potential to regulate the balance between immune activation and tolerance. While deregulation of miRNA expression has been reported in SLE, little is known about the mechanisms that these changes promote autoimmunity.

**Methods:** TaqMan miRNA arrays were used to examine the expression of 365 miRNAs. The expression of miRNAs and their target genes were validated by real time PCR and Western blot analysis. The effect of mir-21 on anti-CD3/CD28–induced T cell proliferation and cytokine production was examined by transfection assays. T-/ B- lymphocyte co-cultures were set up and plasma cell differentiation was assessed by flow cytometry and anti-nuclear antibody (ANA) measurement.

**Results:** We identified a 27 miRNA signature in SLE patients; 19 miRNAs correlated with disease activity. The identified miRNAs are predicted to regulate genes and processes pertinent to lupus pathogenesis such as DNA methylation, apoptosis, and proliferation. MiR-21 was of the highest up-regulated miRNAs in SLE patients and correlated strongly with lupus disease activity (r2=0.92). Compared to healthy T cells, SLE T cells significantly up-regulated miR-21 upon anti-CD3/CD28–activation and displayed increased proliferation. Silencing of mir-21 decreased their proliferation rate while increased the expression of its target gene PDCD4, a selective protein translation inhibitor. The inverse correlation of mir-21 with PDCD4 expression was further demonstrated in freshly isolated PBMCs from SLE patients and healthy controls. Restoration of PDCD4 levels by silencing mir-21 decreased the production of IL-10 and the expression of membrane CD40L by SLE T lymphocytes. Importantly, antagomir-21–transfected T cells had reduced capacity to drive lupus B cell differentiation into CD19+CD38+IgD- plasma cells. Finally, miR-21 over-expression in normal T cells led to acquision of an activated phenotype.

**Conclusion:** Upregulated miR-21 affects PDCD4 expression and regulates aberrant T cell responses in human lupus that contribute to B cell hyper-responsiveness and thus may represent a potential therapeutic target in this disease. MiRNAs represent potential biomarkers in lupus as their expression reflects underlying pathogenic processes and correlates with disease activity.

## OP-106

### Expression and function of the NLRP3 inflammasome in Greek patients with familial Mediterranean fever

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**Deceased*

**Background:** The NALP3 inflammasome is a multiprotein complex that upon activation produces IL-1b among other inflammatory cytokines. Pyrin, the mutated protein in Familial Mediterranean fever (FMF), is generally considered as a negative regulator of IL-1b production. Although the exact mechanism for this effect is not yet known, it is has been shown that pyrin interacts with the adaptive protein ASC (1), or with caspase-1 (2) or even with NF-κB (3).

Objective: To assess expression and function of NALP3-inflammasome in peripheral blood cells of FMF patients.

**Methods:** EDTA-anticoagulated whole blood from patients and healthy controls was used after RBC lysis. TLR4 was stimulated by LPS (250 pg/ml x 2hrs) and the NALP3-inflammasome was activated by ATP (5mM X 20min). Caspase-1 inhibitor (10μM x 15min) was used to determine inflammasome dependency of IL-1β production. Supernatants were collected prior and following treatments for Elisa, to measure levels of IL-1β and TNF expression, and cell extracts were collected to obtain protein for Western Blotting, using IL-1β, caspase-1 and NALP3 antibodies. Protein densitometry from the Westerns was assessed using the Image J program.

**Results:** We studied 13 FMF patients (3 males) of mean age (43.6 (4.3) years and 10 controls (5males) of mean age 39.2 (1.7) years. All but one patient were asymptomatic at the time of evaluation and all were on treatment with colchicine. At baseline, intracellular expression of NALP3, the 2 isoforms of pre-caspase-1 (caspase-p50 & p37) and of active caspase-1 (p20) were comparable between FMF patients and controls. Baseline secretion of IL-1b was minimal and comparable between patients and controls (3.9 (SEM 0.6) pg/ml vs 2.9 (0.8) pg/ml). The combination of ATP and LPS effectively activated NALP3-inflammasome and IL-1b production (mean 1669 (194) pg/ml) compared to either stimulus alone ($p<0.001$). Upon NALP3-inflammasome activation, FMF patients secreted lower amounts of IL-1b compared to controls (mean 1185 (217) pg/ml vs 2298 (227) pg/ml, $p=0.003$). Activation of NALP3 inflammasome was even less in the active patient (fever, arthritis) (77.8 pg/ml). Caspase-1 specific inhibitor (zYVAD-fmk) down-regulated IL1b production comparably both in patients (50 (2) %) and controls (48 (4) %).

**Conclusions:** Although FMF patients had basal expression of NALP3-inflammasome proteins comparable to controls, they produced lower IL-1b upon NALP3 activation. This could be attributed to cell exhaustion due to chronic activation of the

pathway of IL-1b production. Alternatively, mutant pyrin may interfere with NALP3-inflammasome components and down-regulate caspase-1 activation and IL-1b production.

## OP-201

### Evolution of autoimmune minor salivary gland (MSG) lesions in Sjögren's syndrome (SS)

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**Background:** The MSG lesions of SS patients extend from mild to severe. The prevalence of certain types of infiltrating mononuclear cells (MNC), including total T cells and their subpopulations, B cells, macrophages (MΦ) and interdigitating dendritic cells (iDC) varies according to lesion severity. MSG lesions are generally thought to develop stepwise, starting from mild infiltrates that progress through time. However, studies of sequential biopsies evaluating this progress are missing.

**Objectives:** To evaluate repetitive MSG samples of SS patients and define the evolution of the grade and composition of lesions through time.

**Methods:** 28 SS patients, which agreed to perform second MSG biopsy, were studied. In 24 patients, the first biopsy had been performed at diagnosis. The median interval (range) between the two sequential biopsies was 55 (30-110) months. The evolution of the MSG lesions grade was evaluated by the number of lymphocytic foci/4 mm2 of tissue (biopsy focus score), Tarpley score and the number of total infiltrating MNC/$mm^2$-tissue. The percentage of total T, CD4+-T, CD8+-T, Treg and B cells, M , iDC, follicular DC (fDC) and natural killer (NK) cells to total infiltrating MNC was analyzed immunohistochemically in the entire tissue. General linear model for repeated measures adjusted for biopsy time interval and non-parametric Wilcoxon test for paired observations were used.

**Results:** The biopsy focus score was found to change in 4 patients [1st/2nd biopsy focus score (%-change): 8.2/11.4 (39), 1.8/3.1 (71), 4.0/11.6 (190) and 6.9/2.0 (-71)]; in three of them was followed by a change in Tarpley score (from 3+ to 4+ and 3+ to 2+ in two and one patient, respectively). The number of infiltrating MNC/$mm^2$-tissue was found to increase in 7 patients (% increase 37, 38, 48, 70, 89, 185 and 204) and reduce in 2 patients (% decrease 62 and 68). This progression was not found to associate with biopsy time interval, incidence of the various inflammatory cell types, other histological, demographic and clinical features or therapy. Statistical analysis of all SS samples revealed that the biopsy focus score and MNC number/$mm^2$-tissue did not change significantly between the two sequential biopsies. From the cell populations studied, only the CD4+-T and CD8+-T cell incidence changed through time. The percentage of CD4+/CD3+-T cells was found to significantly decrease in the second biopsy (mean SD in the 1st vs 2nd biopsy: 67.1±8.9 vs 54.6±13.0, p:0.016), whereas the percentage of CD8+/CD3+-T cells to increase (32.9±8.9 vs 45.4±13.0, p:0.016). However, these changes were not found to affect the $CD4^+$/$CD8^+$-T cell ratio (2.2±1.03 vs 1.4±0.9, p:0.09). Other histological parameters, such as fibrosis, fat infiltration or germinal center formation did not differ between the two sequential biopsies. The biopsy time interval was not found to affect the evolution of the lesion grade or composition. Finally, the histological parameters tested were not found to correlate with any demographic, clinical and therapeutic features of patients.

**Conclusions:** In the majority of SS patients, the grade and composition of MSG lesions at diagnosis remained mainly unchanged through follow-up, suggesting that the MSG infiltrates do not significantly progress.

## OP-205

### Takayasu's Arteritis is associated with HLA-B*52, but not with B*51, in Turkey

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**Background:** HLA-B*51 and B*52 are two close HLA alleles with minor amino acid differences. However, they are associated with two different vasculitides (B*51 with Behcet's disease and B*52 with Takayasu's arteritis-TAK) with major clinical and immunological differences.

**Objectives:** This study aimed to screen a large cohort of TAK patients from Turkey for the presence of HLA-B*51 and B*52 as susceptibility and severity factors.

**Methods:** TAK patients (n=330, F/M: 6,9/1, mean age: 37.8 years) followed by 15 centers were included in the study. DNA samples from the patients and healthy controls (n=210) (HC) were isolated and the presence of HLA-B*51 or B*52 was screened by using polymerase chain reaction (PCR) with sequence specific primers (SSP).

**Results:** B*52 has shown a significant association with TAK (20.9% vs. HC: 6.7%, p<0.0001, OR: 3.7). The distribution of B*51 did not differ between TAK and HC (22.7% vs. 24.8%, OR: 0.9). The presence of B*52 decreased in late-onset (>40 years) patients (12.9%, OR: 0.44, p=0.04). Type I angiographic disease with limited aortic involvement also had a lower presence of B*52 compared to other phenotypes (13.1%, p=0.005).

In the logistic regression analysis, older age at disease-onset was significantly associated both with refractory disease (P=0.022, OR: 0.436) and surgery after immunosuppressive drug treatment (p=0.005, OR: 4.76).

**Conclusion:** In this study, the previously reported association of TAK with B*52 in other populations was confirmed in patients from Turkey. B*52 seem to be present mainly in classical TAK (early-onset) with extensive aortic disease. The functional relevance of B*52 in TAK pathogenesis has to be further explored.

## OP-206

### Severe damage assessed by a validated tool in a long-term followed-up Takayasu arteritis cohort

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**Background:** Takayasu arteritis (TA) is a large vessel vasculitis with a chronic course. Damage has already been occured at the time of diagnosis. To our knowledge, there is no reported study assessing the damage related to disease itself or due to treatment, using by a validated damage scoring system.

**Aim:** We aimed to evaluate the damage of TA patients with a generic systemic vasculitis assessment tool of VDI.

**Methods:** Fifty TA patients (45 female) diagnosed according to ACR 1990 criteria and followed-up more than 6 months were enrolled into the study. All patients underwent detailed examination including eye, vascular imaging, echocardiography and bone dansitometry. Clinical, angiographical and treatment characteristics and damage items of VDI were noted into a standardized protocol cross-sectionally. Disease activity assessed by Kerr criteria and quality of life (QoL) evaluated by SF-36 were also considered. Impact of damage on SF-36 was evaluated by correlation analysis and Mann Whitney-U test.

**Results:** The mean age, follow-up time and disease duration were 29.4±10.6 years, 86.3±86.5 months and 129±123 months, respectively. Type I (aortic arc) (46%), V (38%), IV (8%), III (4%), IIa (2%) and IIb (2%) were observed with noted frequencies. Subclavian (86%), carotis (66%), renal (43%), vertebral (38%), superior mesenteric artery (28%), axillary arteries (22%) and abdominal aorta (36%) were the involved arteries. Cumulative dose and duration of glucocorticoids were 12.7± 10.7 g and 85±81 months. TA cohort was exposured to MTX (72%), AZA (42%), CP (8%), MMF (4%) and anti-TNF-alpha (8%). Forty-six% of TA patients were active by Kerr criteria. The damage items were listed in Table 1. The mean VDI scores at the first visit was 5.3±2 (1-10) (4.6±1.7 for disease and 0.7±0.9 for treatment related damage). Mean scores of physical, mental components of SF-36 were 33.5±1.2 and 42.6±1.2. No correlation was demonstrated between damage and SF-36.

**Table (OP-206):** The frequency of VDI items in TA cohort

| Damage Items | Frequency (%) |
|---|---|
| Major vessel stenosis | 98 |
| Claudication >3 mths | 94 |
| Absent pulses in one limb | 86 |
| Diastolic BP ? 95 or requiring antihypertensives | 66 |
| Valvular disease | 36 |
| Osteoporosis/vertebral collapse | 28 |
| Cataract | 20 |
| Pulmonary hypertention | 18 |
| Retinal change | 12 |
| Gonadal failure | 12 |
| Cerebrovascular accident | 8 |
| Myocardial infarction | 8 |
| Estimated/measured GFR □ 50% | 6 |
| Diabetes | 6 |
| Visual impairment/diplopia | 6 |
| 2nd cerebrovascular accident | 4 |
| Avascular necrosis | 4 |
| Significant muscle atrophy or weakness | 4 |
| Cardiomyopathy | 4 |
| Minor tissue loss | 2 |
| Major tissue loss | 2 |
| Complicated venous thrombosis | 2 |
| Cranial nerve lesion | 2 |
| Malignancy | 2 |
| Deforming/erosive arthritis | 2 |
| Hearing loss | 2 |

**Conclusion:** A small group of TA patients who followed-up long-term from a dedicated vasculitis clinic showed mean severe damage scores (≥5) as reported in systemic necrotizing vasculitis. Majority of TA patients had disease related damage, characterized with peripheric vascular involvement. Osteoporosis was the most common treatment related damage. Chronic, progressive disease course might be the reason for the lack of correlation between damage and QoL.This preliminary data should be evaluated by prospective multicentric studies.

## OP-301

### Enhanced atheromatous process in patients with spondyloarthropathy

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**Background:** Ample evidence has been accrued during the past decade that chronic inflammatory arthritides, particularly rheumatoid arthritis, are associated with accelerated athero-

matosis and a higher prevalence of atherothrombotic events compared to the general population. Similar results have been published for patients suffering from spondyloarthropathies (SpA), and, in particular, the two major subsets, ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Our aim was to study the lipid profile of Greek patients with SpA and to seek for evidence of enhanced subclinical atheromatosis.

**Methods:** We conducted a cross-sectional study of non-diabetic patients with Spa followed at the Rheumatology Clinic of the University Hospital of Ioannina. We measured serum lipid and lipoprotein levels of SpA patients and compared the results to those of apparently healthy age- and sex-matched controls. Further, by means of carotid ultrasound we measured and compared the carotid intima-media thickness (IMT) of SpA patients and controls.

**Results:** One hundred and fifty SpA patients [73 with AS, 71 with PsA and 6 with other forms of SpA] and 150 controls were studied. SpA patients had significantly lower levels of cholesterol (p=0.032), triglycerides (p=0.018) and high density lipoprotein cholesterol (HDL) (p<0.001), a higher cholesterol/HDL ratio (p=0.007), lower levels of Apolipoprotein B (ApoB) (p<0.001), ApoE (p<0.001), Lp(·) (p=0.02) and a lower ApoB/ApoAI ratio (p=0.003). When PsA and AS patients were examined separately, a particular pattern of dyslipidemia involving lower HDL and a higher cholesterol/HDL ratio was a recurring finding. Correlation analyses in the whole SpA group revealed a statistically significant inverse association of erythrocyte sedimentation rate (ESR) with HDL (r=-0.222, p=0.003) and ApoAI (r=-0.224, p=0.003). In the PsA subgroup, similar significant correlations also emerged between ESR and HDL (r=-0.362, p<0.001), as well as ApoAI (r=-0.338, p=0.001). Analogous associations were observed between C-reactive protein (CRP) and the above parameters as well. In the AS subgroup, a correlation of CRP with HDL (r=-0.223, p=0.049) and ApoAI (r=-0.31, p=0.007) was also evident. When we focused on the subgroup of patients with newly diagnosed SpA who had never received anti-rheumatic treatment before (N=41), we found that SpA patients had lower levels of cholesterol (p=0.003), and HDL (p<0.001), but also they had lower levels of the atheroprotective ApoAI (p<0.001) and a higher ApoB/ApoAI ratio (p=0.001). A significant inverse correlation was also found between ApoAI and ESR (r=-0.416, p=0.016) and CRP (r=-0.364, p=0.044) in this subgroup of patients. Finally, carotid ultrasound performed in a random subgroup of SpA patients (N=49) revealed that SpA patients had a significantly higher IMT compared to controls (0.071 cm vs 0.063 cm, p=0.017).

**Conclusions:** SpA patients show a particular type of dyslipidemia characterized mainly by low HDL cholesterol levels and an unfavorable atherogenic index (cholesterol/HDL) as opposed to apparently healthy individuals. This particular lipid perturbation may, at least partly, be driven by inflammation, since in untreated SpA patients the metabolic disturbance is expanded to further involve a depression of the atheroprotective ApoAI levels and an adverse ApoB/ApoAI ratio. Moreover, carotid ultrasound disclosed more advanced atheromatous lesions as assessed with IMT compared to controls.

## OP-303

### High prevalence of axial spondyloarthritis in patients with familial Mediteranean fever, and a greater allelic frequency of M694V in familial Mediteranean fever patients with radiograpic sacroiliitis

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**Background:** Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever and serositis. Limited data suggest that the prevalence of sacroiliitis, which is a hallmark of ankylosing spondylitis (AS), is increased in patients with FMF. Moreover in most recent studies we and other groups have found a significantly higher frequency of M694V in AS patients. Therefore in the present study we assessed the prevalence of axial spondyloarthritis (SpA), including AS, in FMF patients. We also studied the presence of MEFV variants in FMF patients with and without radiographic sacroiliitis.

**Patients and Methods:** The first 258 patients with FMF [130 female (%50.4), mean age 38.9±12] who were invited to the outpatient clinic for another study were interviewed by using a structured questionnaire to capture patients with SpA. Presence of inflammatory back pain (IBP) was judged based on both Calin and Berlin criteria and the diagnosis of AS was based on the modified New York (mNY) criteria. Standard pelvic X-rays of the sacroiliac joints (SIJ) were performed in all patients. Patients with IBP were also assessed by magnetic resonance imaging (MRI) of SIJ and HLA B27 testing . MEFV variants of the patients were extracted from the patients' medical charts.

**Results:** Two hundred FMF patients (108 female; 54%) patients (77.5%) reported to have current and/or past back pain. IBP according to Calin and Berlin criteria were present in 53 patients (26.5%) and 42 patients (21%), respectively. One patient had inflammatory bowel disease and one had psoriasis, and 56 (21.8%) had a positive family history for SpA. A total of 15 patients (5.8%) had radiographic sacroiliitis (bilateral grade 2 or unilateral grade 3-4) and 14 of them fulfilled the mNY criteria for AS. Additionally bone marrow edema was detected by MRI of SIJ in 13 patients with IBP (5.0%). HLA-B27 positivity was found in only one of the 12 patients with sacroiliitis on MRI and in none of the 14 patients with radiographic sacroiliitis. Allele frequency of M694V in FMF patients with radiographic sacroiliitis was significantly higher in comparison to

those without sacroiliitis (67.9% vs 43.7%; p=0.017) with an OR of 2.7 (95% CI= 1.2 to 6.2).

**Table (OP-303):** Characteristics of patients with sacroiliitis

| | |
|---|---|
| Age, years, mean±SD | 41.1±11.5 |
| Female, n (%) | 9 (60) |
| Age at onset of FMF; years, mean±SD | 12.4±5.2 |
| Age at onset of back pain; years, mean±SD | 31.6±11.6 |
| BASDAI, mean±SD | 3.5±2.3 |
| BASFI, mean±SD | 2.0±1.8 |
| Presence of syndesmophyte, n (%) | 3/14 (21) |
| HLA-B27 positivity, n (%) | 0 (0) |
| M694V positivity, n (%) | 12 (85)* |

*Based on 14 unrelated cases.

**Conclusion:** Our results suggest that axial SpA in patients with FMF and SpA is more common than in the general population. Moreover, M694V may be playing a bigger role than HLA-B27 in susceptibility to AS in FMF patients.

## OP-304

### Prevalence of FMF and chronic renal failure due to amyloidosis and frequency of MEFV mutations in Zara, Turkey

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**Background:** We had previously observed that a good proportion of our FMF patients originated from Sivas Zara, a small city in Central Anatolia. It is also known that many people from Zara have migrated to other cities and countries.

**Objectives:** The aim of this study was to determine the prevalence of FMF, renal failure due to amyloidosis and the carrier frequency of MEFV mutations, both in people who live in Zara and those who have migrated, to study the role of both genetic and environmental factors in FMF.

**Methods:** 15906 people between the ages of 18-60 live in Zara. To detect a prevalence of 0.6% with an error of 0.35% and 95% CI we calculated that we should screen 1673 people. Only the index person was interviewed in each house with a questionnaire for her/himself and another questionnaire for family members between the ages of 10-70. Subjects with recurrent abdominal and/or chest pain associated with fever which disappeared between the attacks, and/or recurrent attacks of arthritis with erythema over the joint were defined as suspected FMF. These subjects were revisited by 6 rheumatologists to ascertain the diagnosis in the second stage of the study. MEFV mutations were studied with sequencing in a 25% sample of index cases.

**Results:** A total of 1727 index people (176 men, 1551 women, mean age: 40.2±11.4) were interviewed. This interview also sought information on 4591 family members (2939 men, 1652 women, mean age: 33.5±19.6). 9 index people (0.5%) and 29 family members (0.6%) already had a diagnosis of FMF. According to the results of the questionnaire, 384/6318 (165 index, 219 family members) had suspected FMF. 348/384 (90%) could be contacted in the second visit. Those who already had a diagnosis of FMF were also examined to confirm the diagnosis. A total of 56/6318 people (0.88%) had definite, 25/6318 (0.39%) had probable FMF. Colchicine was started in these 2 groups. Additional tests were inquired from 26/6318 (0.41%) people who were still not determined. Among the general population who were studied for MEFV mutations 101/230 (44%) had a mutation on exon 2 or exon 10. Among these 12 were M694V. The frequency of dialysis in Zara was significantly higher than the overall frequency in Turkey (12/6318, 0.19% vs 39.267/70.586.256, 0.06%; p<0.001). Among the 12 dialysis patients 3 had a diagnosis of FMF and 1 had probable FMF.

**Conclusions:** Based on these results, the minimal prevalence of FMF in Zara is at least 0.9%. Inclusion of probable cases would increase it to 1.3%. The frequency of dialysis is higher than the overall frequency for Turkey. At least 25.0% of dialysis patients in Zara have FMF.

## OP-306

### Is early diagnosis of pulmonary arterial hypertension possible in inflammatory rheumatic diseases? Experience of a single centre from Turkey

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**Introduction:** Pulmonary arterial hypertension (PAH) is a devastating complication of inflammatory rheumatic diseases. The aim of this study is to determine the role of screeening for the early diagnosis of pulmonary hypertension (PH) in inflammatory rheumatic diseases.

**Method:** Data of the patients with inflammatory rheumatic diseases and PH who had no obvious cause of PH and evaluated by Study Group for Pulmonary Hypertension in Hacettepe

University were investigated retrospectively. All the patients with inflammatory disease were evaluated with right heart catheterization (RHC) if they had systolic pulmonary arterial pressure (sPAP) ≥40 mmHg and/or symptoms related to PH unless explained with other causes.

**Results:** Right heart catheterization was performed in 47 patients with inflammatory rheumatic diseases and PH among 50 who were planned to be evaluated with RHC based on clinical and Doppler echocardiographic findings. There was a positive correlation between sPAP pressure estimated by Doppler echocardiography and sPAP determined with RHC in patients with inflammatory rheumatic diseases (r=0.66; p<0.001) though mean pulmonary arterial pressure were found to be < 25 mmHg in 27.7% of the patients. New York Heart Association functional capacity (NYHA FC) was class III or IV in 79.0 % of the patients with PAH. PAH was more frequent in patients with NYHA FC III-IV in comparison to patients with NYHA FC I-II (58.7% (15) patients vs 19.0% (4) patients; p=0.009).

**Coclusion:** In this study about 80 % of the patients with inflammatory disease associated PAH were diagnosed late in NYHA FC III or IV. There are still unresolved issues in the diagnosis and treatment of PH in inflammatory diseases. Collaboration and multidisciplinary approach is the key point to overcome the challenges in this field.

## OP-401

### Anti-TNF therapy improves insulin resistance and restores insulin signaling in patients with rheumatoid arthritis

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**Background:** Prevalence of insulin resistance and metabolic syndrome has been reported to be high in rheumatoid arthritis (RA) patients. Tumor necrosis factor (TNF), may promote insulin resistance by inducing $Ser^{312}$ phosphorylation (p-Ser312) of insulin receptor substrate (IRS)-1 and downregulating phosphorylated (p-)AKT. We examined whether anti-TNF therapy improves insulin resistance in RA patients and changes insulin signaling cascade.

**Methods:** Prospective study of RA patients receiving anti-TNF agents (n=61) due to high disease activity. Insulin resistance, insulin sensitivity and pancreatic beta cell function were measured by the Homeostasis Model Assessment (HOMA-IR), the Quantitative Insulin Sensitivity Check Index (QUICKI) and the HOMA-B respectively. Protein extracts from peripheral blood mononuclear cells were assayed by western blot for p-Ser312 IRS-1 and p-AKT. RA patients treated with abatacept (CTLA4.Ig) were used as controls for insulin signaling studies.

**Results:** After 12 weeks of anti-TNF therapy, patients with high insulin resistance demonstrated reduction in HOMA-IR (p<0.001), HOMA-B (p=0.001), serum triglycerides (p=0.039), and increase in QUICKI (p<0.001) and serum HDL-C (p= 0.022). Western blot analysis in seven RA patients with high insulin resistance showed reduction in p-$Ser^{312}$ IRS-1 (p= 0.043) and increase in p-AKT (p=0.001). In contrast, the effect of CTLA4.Ig on p-$Ser^{312}$ IRS-1 and p-AKT levels was variable.

**Conclusions:** Anti-TNF therapy improved insulin sensitivity and reversed defects of insulin signaling cascade in RA patients with active disease and high insulin resistance, supporting a beneficial role for TNF inhibition in reducing the cardiovascular disease burden in active RA.

## OP-402

### Therapeutic approaches of patients with inflammatory arthritis and hepatitis B virus (A+HBV study): a national multicentric study

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**Background:** There is no definitive consensus about anti-viral prevention and DMARDs/biological therapy in patients with inflammatory arthritis (IA) and hepatitis B virus (HBV) infection. Objective of this study was to assess the using DMARDs/biological therapy with or without anti-viral prophylaxis in HBV infection according to HBV viral load.

**Method:** Patients with IA and HBs Ag (+) were enrolled to this study from 12 different centers. Demographic data, treatment histories (DMARDs, anti-TNF and anti-viral therapy), transaminases, hepatitis markers, HBV viral loads (copy/ml) were noted. Patients who had HBV viral load at baseline and follow-up period were included to study. First HBV viral load date was accepted to beginning point. HBV viral load higher than 104 copy/ml was defined as active HBV state.

**Tablo (OP-402):**

| | All patients (n=80) n (%) | No anti-viral therapy (n=24) n (%) | Concurrently DMARD/ anti-TNF and antiviral ( n=38) n (%) | Anti-viral therapy after DMARD/anti-TNF (n=18) n (%) | p |
|---|---|---|---|---|---|
| (Follow-up duration (months) | 31±22 | 39 ± 27 | 21 ± 16 | 43 ± 21 | <0.001[1,2] |
| RA | 38 (47) | 10 (42) | 15 (39) | 13 (72) | |
| SpA | 39 (49) | 12 (50) | 22 (58) | 5 (28) | >0.05 |
| JRA | 3 (4) | 2 (8) | 1 (3) | 0 (0) | |
| MTX | 48 (60) | 14 (58) | 20 (53) | 14 (78) | |
| SSZ | 45 (56) | 17 (71) | 20 (53) | 8 (44) | >0.05 |
| Leflunomide | 13 (16) | 3 (12) | 6 (16) | 4 (22) | |
| ETN | 18 (22) | 6 (25) | 6 (16) | 6 (33) | |
| INF | 14 (18) | 4 (17) | 4 (11) | 6 (33) | |
| ADA | 9 (11) | 1 (4) | 7 (18) | 1 (6) | |
| Transaminases (beginning/follow-up) | | | | | |
| Normal | 71/68 | 23/20 | 35/33 | 13/15 | 0.03[3] |
| 1-1.5x | 3/2 | 1/ 0 | 1/1 | 1/1 | 0.047[2] |
| 1.5-3x | 3/5 | 0/2 | 2/3 | 1/0 | |
| 3-5x | 0/3 | 0/1 | 0/1 | 0/1 | |
| >5x | 3/2 | 0/1 | 0/0 | 3/1 | |
| HBV-DNA (beginning/follow-up) | | | | | |
| n/n | 52 (65) | 16 (67) | 26 (68) | 10 (56) | >0.05 |
| n/↑ | 11 (13) | 3 (12) | 3 (8) | 5 (28) | |
| ↑/n | 10 (12) | 1 (4) | 6 (16) | 3 (16) | |
| ↑/↑ | 7 (10) | 4 (17) | 3 (8) | 0 (0) | |

[1]Anti-viral (-) vs antiviral (+) at the beginning, [2]Antiviral (+) at the beginning vs anti-viral (+) later, [3]Anti-viral (-) vs anti-viral later

**Results:** Eighty (male/female: 40/40) patients, mean age 44±12 years old and mean follow-up duration 31±22 months were enrolled (Table). Hepatitis markers were as follow; HBsAg 80 (100%), HBeAg 7 (8.7%), anti-HBs 0 (0%), anti-HBe 49 (61.3%), anti-HBc 50 (62.5%). Fiftysix patients (70%) [38 (47%) patients concurrently used DMARDs/biological agents with anti-viral, 18 (23%) patients used anti-viral therapy after DMARDs/biological agents, (Table)] were taken anti-viral prophylaxis, median duration was 18.5 (2-84) months. Treatments of patients included; Mtx 48 (60%), SSZ 45 (56%), Leflunomide 13 (16%), ETN 18 (22%), INF 14 (18%) and ADA 9 (11%). Sixtythree (78%) of patients had normal HBV viral loads at the beginning (Figure). HBV viral loads were increased in 11 (17.4%) of patients [only 3 patients had increaed transaminases level]. Seven of those 11 (63.6%) patients used anti-TNF therapy: 2/18 (%11) ETN (one with

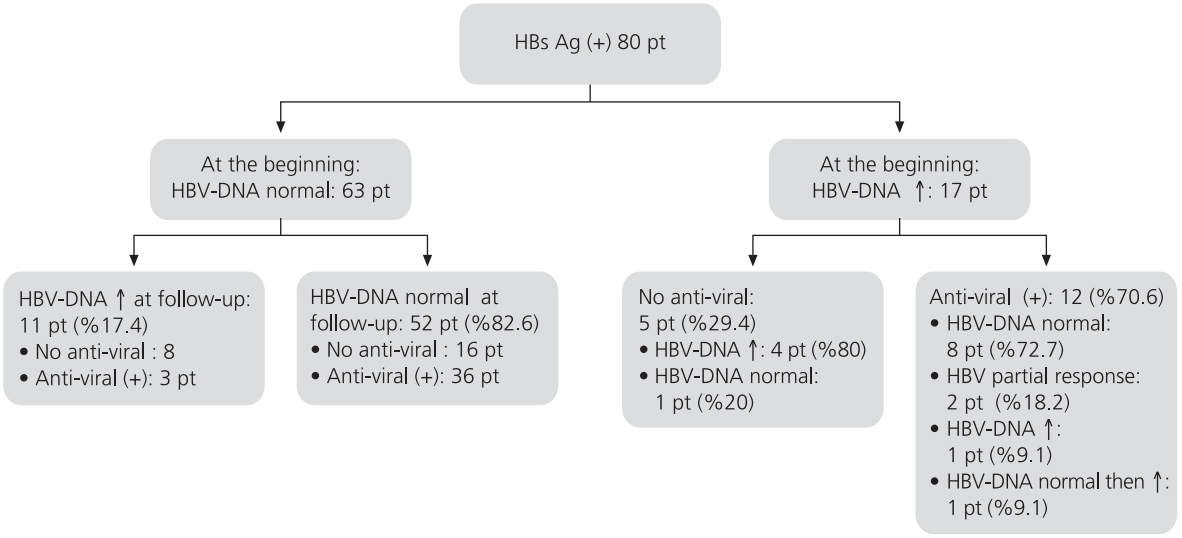


**Figure (OP-402):**

anti-viral, one without), 2/14 (%14.2) INF (none with anti-viral), 3/9 (%33) ADA (2 with anti-viral, one without). At the beginning of DMARDs/biological therapy 17 patients had increased HBV viral load (HBV load > 105 in 8 patients), however only 2 patients had increased transaminases levels. Twelve of 17 patients were taken anti-viral prophylaxis (Figure).

**Discussion:** This study shown that there was different approach to HBV infection in rheumatology experts from different centers. Approximately half of the patients were not given anti-viral prevention at the beginning of DMARDs/biological agents. On the other hand, viral replication was found in 17% of patients, most of these patients were under anti-TNF therapy. Transaminases were not useful for follow-up of those patients and HBV viral load needs to be followed clinical practice.

## OP-404

### How many patients do we really need to enroll in RA RCT? An analysis of published trials

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**Objective:** Randomized controlled trials (RCT) are designed to answer specific questions using a certain number of patients, determined by sample size calculation. If the calculation is not done properly, more than the needed number of patients may be enrolled, leading to unnecessary exposure for those patients to potentially harmful drugs. In an ideal world, assumptions that go into the calculation of the sample size would be more certain. However in the real world it is not always possible to have ideal calculations and it would be expected that under and over enrolling would be seen in roughly similar number of RCTs.

**Methods:** A Pubmed search was conducted, for RCT of abatacept, etanercept infliximab, rituximab and tocilizumab, in rheumatoid arthritis (RA) patients (n=241). Only original initial studies where the primary outcome was efficacy were analyzed (n=34). Using the final results for the primary outcome, back calculation of the actually needed number of patients for the trials were calculated and compared to the actual enrollment numbers.

**Results:** 34 studies were analyzed (infliximab 10, etanercept 7, abatacept 7, tocilizumab 5, rituximab 5). Primer efficacy outcome was ACR 20 in 24 studies. ACR 50 in 2 studies, ACR N in 2 studies, DAS-28 in 4 studies, Paulus 20 in 2 studies and reduction of number of swollen/tender joints in 1 study. The mean number of patients enrolled in the treatment arms was 164 and the control arms was 116. After back calculation, the actual needed numbers for the treatment arm was 86 and control arm was 86. According to the recalculated sample size results, there were more patient than required to show differences between groups in 27 studies (79%) and less patients than required in 7 studies. In the 27 studies were more than necessary patients were enrolled had a median of 101 extra patients (mean: 196.19±241.44).

**Conclusion:** 4/5 RCT of biologic agents in the treatment of RA had on average at least 100 patients unnecessarily enrolled. This was a trend seen regardless of agent or how many previous RCT had been done with the same agent. It is an ethical obligation to conduct a RCT with only the necessary number of patients to answer the scientific question that is being asked. Our data suggests that most RCT fall short of this standard.

## OP-405

### Long-term survival of anti-TNF agents in rheumatoid arthritis: data from the Hellenic Registry of Biologic Agents

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**Background:** Although anti-TNFα agents have been effective for the treatment of Rheumatoid Arthritis (RA), treatment discontinuation is not rare.

**Objective:** To study the long-term survival of anti-TNF agents in rheumatoid arthritis and to determine the reasons for stopping treatment.

**Methods:** This study is based on data from the Hellenic Biologic Registry for Rheumatic Diseases, Data on efficacy and safety are recorded from 7 Academic and State Rheumatology clinics in Greece. Demographics, disease characteristics and treatments are recorded according to a standardized evaluation protocol (based on the South Swedish Arthritis Treatment Group protocol). The reason for stopping therapy is categorized to response failure, adverse effect, and others like patient decision, pregnancy wish etc.

**Results:** 998 patients with RA were analyzed (age 57.4±42 yo, disease duration: 10.1±9 years, DAS28 baseline: 5.8±1.2). Patients started treatment with infliximab (53%), adalimumab (29%) or etanercept (18%) and were followed up for a total of 3114 patient/years. 10.2% of the patients had stopped treatment at the first six months, 20.2% at 12 months, 33.8% at 24 months, 44.5% at 36 months and 55.7% at 48 months of follow up. The most common reason for stopping was response failure at the first 6 (48.5% of stopping) and 12 months (46.2%of stopping), while an adverse event was the most common reason for stopping therapy at the third (47.2% of stopping) and fourth year (36%) of follow up (Table 1). The rate of stopping was higher for infliximab (12.8 stops/100 patient/years) and the most common reason was an adverse event (mostly infusion reactions) (Table 2).

**Table 1 (OP-405):**

| Follow up/ months | On therapy | Stop Failure | Stop AE | Stop other |
|---|---|---|---|---|
| 0 | 998 | 0 | 0 | 0 |
| 6 | 838 | 46 | 39 | 10 |
| 12 | 691 | 83 | 74 | 18 |
| 24 | 496 | 118 | 107 | 28 |
| 36 | 361 | 131 | 124 | 34 |
| 48 | 267 | 147 | 141 | 48 |

The rates of stopping for adalimumab and etanercept were 10.8 and 9.2 stops/100 patients/year respectively treatment failure was the most common reason for stopping. The main events that caused treatment discontinuation besides infusion reactions (40.6%) were infections (19%) and cancer (17%).

**Table 2 (OP-405):** Discontinuation rate (stop/100 patients/year)

| | All | Adverse event | Failure | Other |
|---|---|---|---|---|
| Infliximab | 12.8 | 6 | 4.3 | 2.5 |
| Adalimumab | 10.8 | 2.3 | 6 | 2.5 |
| Etanercept | 9.2 | 3 | 5.1 | 1.1 |

**Conclusions:** Survival of the first anti-TNF biologic therapy in RA patients is reduced significantly after the third year of follow up. Infliximab has the shorter drug survival, mostly due infusion reactions.

## OP-406

### Gender differences of ankylosing spondylitis patients receiving anti-TNF therapy

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**Background:** To compare clinical and laboratory parameters in male and female patients with ankylosing spondylitis (AS) receiving anti-TNF therapy.

**Methods:** This report retrospectively evaluated the data of 146 patients with AS fulfilling modified New York criteria, who were followed between 2001 and 2010. The medical records included demographic characteristics, clinical symptoms, physical examination (Schober's test, finger-to-floor distance, chest expansion), laboratory findings (ESR, CRP, HLA-B27), complications and therapies. Values were compared within groups using Student's t test.

**Results:** The mean age, age at symptom onset, delay in diagnosis, disease duration (year) were 43.6±11.6, 28.3±11, 7.2, 15.3 in females and 38.5±10.2, 22.7±10.2, 5.3, 16 in males respectively. The mean age at symptom onset was significantly lower in males (*p<0.01). The time interval between the onset of symptoms and anti-TNF therapy (year) >10, 5-10, <5 were 55 (54%), 35 (34%), 12 (12%) in males and 22 (50%), 27 (27%), 10(23%) in females respectively. The mean duration of treatment was 28 months in both groups. HLA-B27 was more frequent in males (90 vs 75%). Peripheral arthritis was more frequent in females (80% vs 55%). Baseline Schober's test (cm), finger-to-floor distance (cm), ESR (mm/h), CRP(mg/L) values were 2.7, 23.6, 45.5, 33.7 in males, and 3.4, 11.5, 45.2, 18.8 in females respectively. After biological treatment, the values were 3.1, 24.5, 19, 9.2 in males, and 2.6, 6.7, 35, 13.9 in females respectively. The mean value of finger-to-floor distance was significantly higher (p<0.001) in males. Initiation of anti-TNF agent due to axial involvement and high inflammatory markers were similar in females and males (96% vs 99%, 48% vs 52%), peripheral arthritis and resistant uveitis were more frequent in females (66 vs 37% and 4.5 vs 2%) whereas proteinuria/amyloidosis was more frequent in males. The termination of anti-TNF therapy due to remission was higher in females (9.1 vs 2%) and termination due to complications was higher in males (2.3 vs 5.9%).

**Conclusions:** These data suggest that diagnosis of AS was delayed both in male and female patients receiving anti-TNF therapy. Biologic therapies did not change the axial measurements significantly, but had positive effects on clinical and laboratory findings. Males were younger, had dominantly axial involvement, whereas females had a higher frequency of peripheral arthritis and better response to treatment.

## OP-407

### Division of Rheumatology, Diyarbakır Goverment Hospital, Diyarbakır; Disease outcomes in a Turkish cohort with early-undifferentiated inflammatory arthritis and the performance of new and old classification criteria for rheumatoid arthritis

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**Background/Purpose:** In rheumatology clinical practice, the majority of patients who present with recent–onset arthritis have undifferentiated arthritis (UA), which is defined as a form of arthritis that does not fulfill the classification criteria for a more definitive diagnosis. It has been demonstrated that approximately one–third of these patients experience spontaneous remission while others remain as undifferentiated or develop rheumatoid arthritis (RA). On the other hand, some forms of arthritis like familial Mediterranean fever (FMF) and Behçet's disease (BD),

are almost unique to the given geographical region and these diseases were not included to cohorts of other countries. The aims of our study were, to determine the disease outcomes of patients with recent onset undifferentiated arthritis and to assess the sensitivity of ACR 1987 revised criteria and ACR/EULAR 2010 criteria for classification of RA.

**Method:** From July 2009 to April 2010, patients with arthritis involving at least 1 joint who did not not fulfill the classification criteria of a specific diagnosis, and duration of the symptoms shorter than 6 months were included to study. Since ACR/EULAR classification criteria were not published at the time of the study initiation, ACR 1987 revised criteria were used. Demographic, clinical and laboratory features of all enrolled patients were recorded. All patients were reassessed at 6th and 12th months. Disease outcomes were determined and rates of patients fullfilling the old and new criteria for RA were compared. Baseline clinical, demograpic and laboratory features of patients with RA and the others were compared.

**Result:** At the beginning of the cohort, according to the inclusion cirteria no patient was fullfilling the ACR 1987 revised criteria for RA, while 16 patients (17.8 %) were met the ACR-EULAR 2010 criteria. After 12-month follow-up, the numbers of patients fulfilling these criteria were 28 (1987) and 45 (2010), respectively. Number of patients diagnosed as spondylarthritis, BD and FMF were 2, 2 and 3, respectively and remission was occured in 22 patients (24.4 %). Comparison of baseline clinical and laboratory features of RA and non-RA patients disclosed that the frequencies of small joint involvement, RF and anti–CCP positivity, symmetrical pattern, tender and swollen joint count were found to be higher in RA group (for each, $p<0.05$). On the other hand, large joint involvement was significantly higher in non-RA group ($p<0.05$).

**Conclusion:** The present study has confirmed the satisfactory sensitivity of new RA classification criteria in our cohort of patients having early arthritis. In patients with large joint involvement, FMF and BD should be kept in mind in the differential diagnosis of UA, particularly in countries where these diseases seen widely. Small joint involvement and positive serological tests are main indicators for predicting the development of RA.

# Poster Presentations

## (PP-01 — PP-08)

### PP-01

### Genetic association with systemic lupus erythematosus in Turkey: A case-control study

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**Background:** Recent genome wide association studies (GWAS) in different populations have detected many SLE-susceptibility genes (1). A significant source of variability in the literature of SLE-susceptibility genes has been the inability to replicate genetic findings across different racial or ethnic groups. We sought to investigate whether a single nucleotide polymorphism (SNP) of the STAT4 (rs7574865) (2), PTPN22 (rs2476601) (3), TRAF1/C5 (rs10818488) (4) and C1q (rs292001) genes as well as the 27-bp VNTR polymorphism on intron-4 of eNOS(5), previously associated with SLE in other populations, are also associated with SLE risk in Turkey.

**Methods:** A group of 158 SLE patients and 155 healthy controls, age- and sex-matched, and a second one of 343 healthy subjects and 305 SLE patients from the island of Crete, were included in this study. Genotyping of the SNPsunder investigation was performed by polymerase chain reaction-restriction fragment length polymorphism (RFLPs) followed by electrophoretic analysis in a 2.5% agarose gel. The statistical significance of the differences observed in allele frequencies within each group of patients and controls examined, was analyzed by chi-square test. Odds ratio and their confidence intervals were calculated according to Rothman.

**Results:** The A/Agenotype and the A allele of the TRAF1/C5 rs10818488 SNP were more frequent in SLE patients (18.35 % and 47.57%, respectively) than in healthy controls(12.26% and 36.45%, respectively). In the case of eNOSgene intron 4 a/b VNTR polymorphism (a 27 base-pair tandem repeat based polymorphism), our results show that the a/a genotype and the a allele were more frequent in cases (8.86% and 24.68%, respectively) than in controls (3.23% and 17.42%, respectively). Patients with SLE presented more commonly with A allele (47.15%) of the of the C1q rs292001 G/A polymorphism than controls (35.81%) ($p=4.0x10-3$, OR=1.60, 95% CI: 1.16-2.20).

No statistically significant difference (p>0.05) in the frequency of the risk allele T of the STAT4rs7574865 and PTPN22rs 2476601 SNPs was observed between SLE patients and controls. Interestingly, the T/T genotype of the STAT4 SNP (p=0.02, OR=3.5, 95% CI 1.21-10.25) was more frequent in SLE patients than in controls, thus indicating association between this genotype with susceptibility for SLE.

**Conclusions:** Although STAT4, PTPN22and eNOSwere found to confer a remarkable degree of risk for the development of SLE in many racial or ethnic groups, in this report only the genetic association of eNOSwith SLE was confirmed in a Turkish population. Moreover, theTRAF1/C5 and C1q gene polymorphisms were also found to confer a degree of risk for SLE. These findings highlight the importance of comparative studies that should be carried out in various populations to confirm the genetic association detected.

## PP-02

### VEGFR2 is involved in systemic lupus erythematosus: A genetic, cellular and structural biological approach

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**Background:** The vascular endothelial growth factor receptor 2 (VEGFR2) regulates the formation of blood vessels through its effects on vascular endothelial cells. VEGFR2 gene polymorphisms correlate with vascular diseases such as coronary heart disease and may influence endothelial integrity, repair and function.

**Objectives:** a) To investigate the role of two functional VEGFR2 gene polymorphisms in systemic lupus erythematosus (SLE); b) To measure the circulating endothelial cells (CECs) in peripheral blood as a surrogate marker of vascular damage and correlate this with gene polymorphisms; and c) To localize the VEGFR2 mutations under study on a constructed three-dimensional (3-D) model aiming to gain insights on their functional role.

**Methods:** The V297I (rs2305948) and H472Q (rs1870377) single nucleotide polymorphisms (SNPs) in VEGFR2 were genotyped with Taqman technology and RFLPs in 150 SLE patients and 96 healthy controls. CECs were isolated from whole blood from 64 SLE patients with CD146-coated magnetic beads and enumerated after staining with TRITC-labeled Aglutinin-1. Modeling of the mutation V297I was based on the 3-D structure of domains D2 and D3 of VEGFR2 in complex with VEGF-C. Sequence alignment of the D5 domain of VEGFR2 was performed on the KIT sequence, followed by homology modeling on the KIT ectodomain structure to investigate mutation H472Q.

**Results:** The risk allele A of the VEGFR2 rs1870377 SNP was more frequent in individuals with SLE than in healthy controls (p<0.0001 OR=2.6, 95% CI 1.7 to 3.9), while A/A genotype appeared to be a SLE risk factor (p=0.0001, OR=5.4, 95% CI 2.14-13.62). No association was detected between rs2305948 and SLE. Within the rs1870377 A/A genotype (n=15) the number of CECs (mean ± SD, 34.4±4) was also significantly higher than that of T/T genotype (N=5, mean±S.D. 11±3, p=0.001). Modeling revealed that amino acid position #297 is located on the D3 Ig-like domain of the extracellular region of VEGFR2 on a surface loop and mutation V297I affects the efficiency of trans-autophosphorylation and cell signaling. Position #472 is located on the surface of the D5 Ig-like domain; mutation H472Q affects homotypic contacts of membrane proximal Ig-like domains and may interfere with ligand-binding.

**Conclusions:** The VEGFR2 H472Q polymorphism is associated with increased susceptibility to SLE, thus implicating VEGFR2 in pathogenesis of the disease. The risk genotype for rs1870377 SNP was associated with higher CECs numbers, indicating that this mutation may correlate with increased endothelial damage. Structural data suggest that both mutations may cause impairment in cell signaling, by increasing VEGF binding to VEGFR2, thus contributing to SLE pathogenesis.

## PP-03

### The importance of interleukin-23 and interleukin-17 in the patients with systemic sclerosis

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**Objective:** To investigate the relation between clinical and autoantibody subsets profiles of systemic sclerosis (SSc) and the levels of serum interleukin (IL)-17 and IL-23.

**Methods:** Forty patients with SSc and forty healthy control subjects were included in the study. Autoantibody profiles and internal organ involvement of the patients with SSc were determined. Modified Rodnan skin scores (MRSS) of the patients were calculated. Serum IL-17 and IL-23 levels were measured by enzyme linked immunosorbent assay (ELISA).

**Results:** Of the scleroderma patients, 24 patients had limited SSc and 16 patients had diffuse SSc. The patients had a mean MRSS of 13.15. Of all the patients, 21 (52.5%) had lung involvement and 16 (40%) had gastrointestinal involvement.

Thirty-six (90%) patients were with ANA positive, 21 (52.5%) were with anti-Scl-70 antibody positive, 6 (15%) were with anti-centromere antibody positive. The mean IL-17 levels of the patient group and control group were respectively 0.67±0.55pg/ml and 0.52±0.10 pg/ml (p=0.007). Whereas, the mean of IL-23 levels of healthy control groups and patients were found to be 30.27±12.68pg/ml and 29.32±10.52pg/ml, respectively (p=0.60). When IL-17 and IL-23 levels were examined in clinical subsets SSc, it was found that the IL-17 levels of dSSc and lSSc groups were 0.70±0.46pg/ml and 0.65±0.61 pg/ml, respectively, whereas the IL-23 levels were 29.46±13.67 pg/ml and 29.22± 8.10 pg/ml, respectively (p=0.65). Any statistically significant difference between modified Rodnan skin score and IL-17/IL-23 levels were not detected. (p:0.142 and 0.668). The relation between serum levels of IL-17/ IL-23 and age, pulmonary and gastrointestinal involvement, disease severity, autoantibody profiles was not found. The levels of plasma IL-17 differed significantly in SSc and control groups but not so in IL-23. There was no association of serum IL-17 and IL-23 levels with clinical and autoantibody subsets.

**Conclusion:** In our study we concluded that IL-17 is associated with SSc, but not with IL-23. In the investigation of IL-17 and IL-23 levels, the studies are propagated regardless of the patients' treatment. To eliminate the difference between studies, the role of cytokine on etiopathogenesis in treated and untreated patients should be inquired. Serum IL-17 and IL-23 levels in SSc patients may also be affected depending on whether the patients had immunosuppressive therapy.

## PP-04

### Microchimerism in Turkish women patients with systemic sclerosis

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**Objectives:** We aimed to investigate microchimerism in peripheral blood lymphocytes from patients with diffuse (dcSSc) and limited (lcSSc) type scleroderma, by examining the sex of the child and patient and gravidity/parity. In addition, we intended to research the association between microchimerism and the clinical subsets.

**Methods:** 50 female patients with lcSSc, 30 female patients with dcSSc and 40 healthy controls were included in the study. Patients and controls were questioned about pregnancy, having son or daughter, obstetric and abortion history. People who had blood transfusion and allogeneic stem cell transplantation were not included in this study. Those with a history of autoimmune disease and drug use in the control group were also excluded. Autoantibody profiles and organ involvements of patients with systemic sclerosis were determined. Modified Rodnan skin scores and Medsger damage index of patients with systemic sclerosis were calculated. Y-chromosome sequences were studied by real time-PCR in DNA that was obtained from peripheral blood mononuclear cells (PBMC).

**Results:** The mean age of patients with lcSSc and with dcSSc were 46.20±14.69 years and 47.23±14.17 years, respectively. The mean age of the control group was 42.55±11.40 years. The age difference between study groups was not statistically significant. Microchimerism was found positive in 28 of 80 patients (35%) and in 8 of 40 healthy controls (20%). Microchimerism was found positive in 6 dcSSc patients who had sons (27.3%), in 10 lcSSc patients with sons (32.3%) and in 7 people who had sons in the control group (18.9%). The difference was not statistically significant (p> 0.05). Microchimerism was detected in 6 nulliparous patients (31.6%) of the lcSSc group and in one nulliparous patient (11.1%) of the dcSSc group (p>0.05) (Table&Figure). The nulliparous patient with dcSSc was 76 years old and the oldest nulliparous patient in the lcSSc group was 60 years old. The mean of the time elapsing between the first pregnancy and diagnosis was 3.5 (0-49) years in microchimerism positive and 14 (0-55) years in microchimerism negative. The difference was statistically significant (Mann-Whitney test, p= 0.020). The means of Modified Rodnan skin scores of patients with and without microchimerism were 10 (4-24) and 13 (4-26), respectively. This was statistically significant (p=0.038). However, the relation between microchimerism and other system involvements, disease severity, autoantibody profiles, children numbers, children ages were not found.

**Conclusions:** Various etiological factors rather than one play role on the development of scleroderma. The presence of microchimerism is thought to be a reason that shortens the elapsing time of disease development.

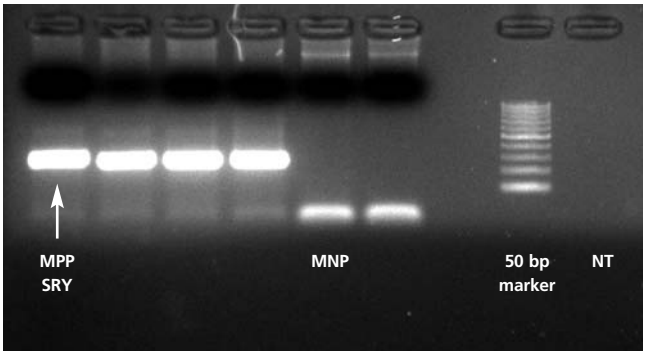


**Figure (PP-04):** Microchimerism according to SRY on agarous gel electrophoresis. MPP: Microchimerism positive patients; MNP: Microchimerism negative patients; NT: Non-templated, negative control with water; SRY: Sex-determining region of Y.

**Table (PP-04):** Characteristic features and microchimerism status of groups.

| | DcSSc | LcSSc | Control | P |
|---|---|---|---|---|
| N (%) | 30 (37.5) | 50 (62.5) | 40 | |
| Age (years) | 47.23±14.17 (44) | 46.20±14.69 (44) | 42.55±11.40 (40) | 0.375 |
| Age at first birth (yrs) | 24.92±5.176 | 24.11±3.889 | 26.21±3.819 | 0.095 |
| Age at diagnosis (yrs) | 36.10±11.89 (33.5) | 40.14±14.23 (37.5) | | 0.188 |
| Time between birth to diagnosis (yrs) | 10.2±9.4 (7.5) | 14.32±14 (12) | | 0.390 |
| Disease duration (yrs) | 11.47±8.9 (9) | 6.20±6.5 (4) | | 0.001* |
| Number of children | 2.69±1.3 (1-6) | 2.76±1.2 (1-6) | 1.74±0.9 (1-5) | <0.05* |
| Pregnancy history | | | | |
| Mothers who had boys n (%) | 22 (73.3) | 31 (62) | 37 (92.5) | 0.004* |
| Mothers who had girls n (%) | 4 (13.3) | 7 (14) | 2 (5) | |
| Nulliparous patients n (%) | 2 (6.6) | 10 (20) | | |
| Patients who had abortionş n (%) | | 2 (4) | | |
| Microchimerism n (%) | | | | |
| Mothers who had boys n (%) | 6 (66.7) | 10 (52.6) | 7 (18.9) | |
| Mothers who had girls n (%) | 2 (22.2) | 2 (10.5) | | |
| Nulliparous patients n (%) | 1 (11.1) | 6 (31.6) | | |
| Patients who had abortionş n (%) | | 1 (5.3) | | >0.05 |

Data expressed in mean±SD (median); DcSSc, diffuse cutaneous systemic sclerosis; LcSSc, limited cutaneous systemic sclerosis; *Statistically significant

## PP-06

### Effect of regular colchicine treatment on biomarkers related with atherosclerosis in newly diagnosed patients with familial mediterranean fever

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**Background:** In recent years increasing number of reports revealed an enhanced early atherosclerosis in patients with familial Mediterranean fever (FMF). Atherogenesis is a complex process which involves vascular injury, increased expression of cellular adhesion molecules, lipid accumulation, heamostatic changes, vascular smooth muscle cell migration and proliferation.

**Objectives:** To evaluate the concentrations of the cellular adhesion molecules (CAMs) including soluble intercellular adhesion molecule-1 (sICAM-1) and soluble CD146 (sCD146), plasminogen activator inhibitor-1 (PAI-1) and fetuin-A in newly diagnosed FMF patients and healthy subjects. We also aimed to evaluate the effect of regular colchicine treatment on these molecules.

**Methods:** 19 FMF patients (8M/11F, 33.6±11.8 years) and 19 healthy subjects (11M/8F, 32.2±7.2 years) were studied. FMF patients were evaluated in the attack-free period. After anthropometrical evaluation high sensitive CRP (hsCRP), sICAM-1, sCD146, PAI-1 and fetuin-A were studied in the both patient and control groups. Biochemical assays and anthropometrical assessments were repeated in the patients' group two months after the standard colchicine treatment.

**Results:** Age, sex distribution, waist circumference, body mass index, smoking status and serum lipids were not different between the patient and control groups (p>0.05). In contrast, hsCRP levels were significantly higher in the patients' group than controls (p<0.05, Table). Cellular adhesion molecules (CAMs) were not different between the patient and control groups (p>0.05). On the other hand, fetuin-A and PAI-1 were signifi-

**Table (PP-06):** Comparison of FMF patients, controls, and the effect of colchicine treatment on various biomarkers related with atherosclerosis.

| | FMF patients (n=19) | Healthy controls (n=19) | P1 | Pre-treatment (n=19) | Post-treatment (n=19) | P2 |
|---|---|---|---|---|---|---|
| Hs-CRP (?g/mL) | 3.58±4.8 | 0.8±1.4 | 0.02 | 3.58±4.8 | 1.18±1.4 | 0.02 |
| sICAM-1 (?g/mL) | 2.27±1.5 | 1.57±0.6 | 0.08 | 2.27±1.5 | 1.66±0.97 | 0.02 |
| sCD146 (ng/mL) | 299±99 | 351±115 | 0.1 | 299±99 | 214±96 | 0.01 |
| Fetuin-A (?g/mL) | 0.52±0.11 | 0.40±0.11 | 0.003 | 0.52±0.11 | 0.43±0.12 | 0.04 |
| PAI-1 (ng/mL) | 12.3±2.3 | 10.1±1.23 | 0.001 | 12.3±2.3 | 11±2.7 | 0.04 |

cantly higher in the patients' group than controls (p<0.05, Table). When we compared pre and post-treatment values of these molecules hsCRP, PAI-1, fetuin-A and CAMs (sCD146 and sICAM-1) were significantly reduced after the treatment (p<0.05, Table). Results were presented as mean±standard deviation. Comparison between groups of continuous variables was performed by using the Student t test. P1 indicates the comparisons between FMF patients and healthy controls. P2 indicates the comparisons between pre-treatment and post-treatment patients.

**Conclusions:** Fetuin-A and PAI-1 concentrations were significantly lower than controls. However, CAMs were not different from the healthy subjects. On the other hand, regular colchicine treatment resulted in a significant decrease in the concentrations of CAMs, fetuin-A and PAI-1.

## PP-07

### The efficacy and safety of rituximab in patients with rheumatoid arthritis: a single center experience

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**Statement of purpose:** Autoantibody (RF, anti-CCP) producing B cells play a key role in the course and prognosis of rheumatoid arthritis. Since rituximab selectively targets B cells, it has the potential to be used in this condition. This study was undertaken to evaluate the efficacy and safety of rituximab treatment in a group of patients with rheumatoid arthritis.

**Methods:** This retrospective study included nine female rheumatoid arthritis patients that received rituximab treatment between June 2009 and September 2010. Following parameters were evaluated before and after treatment: tender joint count (TJC), swollen joint count (SJC), visual analogue scale (VAS) score, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and disease activity score (DAS-28). In addition, steroid doses, adverse events (AEs) and serious adverse events (SAEs) were recorded throughout the study period.

**Summary of Findings:** The mean age was 56.6±7.8 years (median 57, range 45-68) and the disease duration was 12±6.28 years (10, 6-22). Two patients had seronegative disease, and the remaining were seropositive for RF and/or anti-CCP. Except one patient, all had received anti-tumor necrosis factor treatment prior to rituximab. The mean number of rituximab treatment courses was 1.2±0.4. Rituximab treatment was associated with significant improvements in VAS score (p=0.015), ESR (p=0.011), CRP (p=0.008), and DAS-28 (p=0.015), but not in TJC (p=0.12) and SJC (p=0.308) (Table, Figure). However, ESR was not decreased normal ranges. Also, patients' quality of life was improved significantly. In addition, rituximab treatment significantly decreased the steroid dose required (p=0.025). The mean time to remission was 4.9±1.5 (6, 2-6) months. No serious adverse events were observed during rituximab infusions. A single patient experienced a minor allergic reaction during infusion that was readily managed with paracetamol and antihistamines.

**Table 2 (PP-07):** Effects of rituximab treatment on disease parameters

| | Before treatment | After treatment | P |
|---|---|---|---|
| TJC | 7.3±2.3 (6) | 2.2±3.8 (.0) | 0.12 |
| SJC | 3±1.4 (2) | 1.5±2.6 (.0) | 0.308 |
| VAS score | 68.9±10.5 (70) | 27.7±23.3 (20) | 0.015* |
| ESR | 67 ± 23.3 (60) | 47.6 ± 27.6 (46) | 0.011* |
| CRP | 31.3±24.08 (23) | 20.4±27.6 (6.6) | 0.008* |
| DAS-28 | 6±0.6 (5.7) | 3.8±1.5 (3.6) | 0.015* |

Data expressed in mean±SD (median)

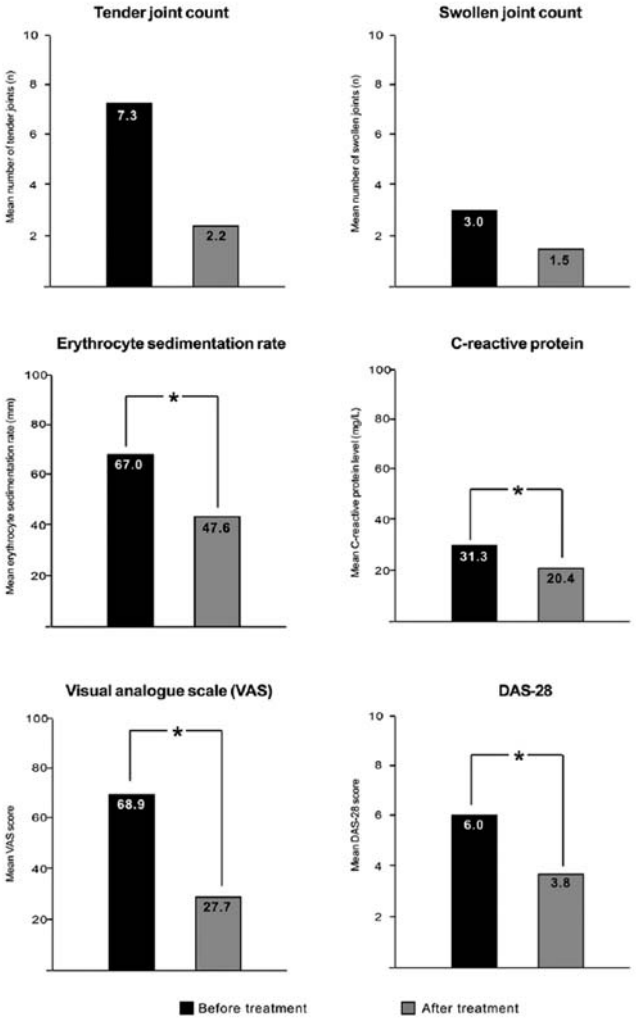


**Figure (PP-07):** Changes in disease parameters after rituximab treatment compared to baseline. *p<0.05

**Conclusions:** In terms of cost-effectiveness, rituximab seems to be better than anti-TNF treatments and it has been successfully used in a number of other conditions. In this study, rituximab was well tolerated, reduced the need for steroids and it was not associated with significant adverse effects in a group of patients with rheumatoid arthritis. Thus, it represents a safe and effective treatment regimen for this condition, particularly in case of resistance to other treatments. We had important limitation that small number of patient.

## PP-08

### Insights form a routine care rheumatoid arthritis registry in Turkey: A quarter of rheumatoid arthritis patients are in remission/low disease activity and on biologic agents

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**Background/Purpose:** New paradigm of early and aggressive approach using combination of methotrexate with biologic agents for inadequate response has led to better outcomes for rheumatoid arthritis (RA), especially documented from randomized clinical trials (RCT). However, real world applicability of these "treating to target" approaches can only be assessed by routine care registries in different populations, with different patient mixes and drug use. TRAV (Turkish acronym for "Turkish Rheumatoid Arthritis Registry") was established in 2010 with the aim of collecting data on RA patients seen in routine care in Turkey, to the best of our knowledge, a first.

**Methods:** Five sites from two different cities in Turkey are currently enrolling patients in TRAV. Three of the sites had data available for this analysis. Consecutive patients seen at the participating centers complete a multidimensional health assessment questionnaire (MDHAQ) at each visit. The MDHAQ includes scales for physical function, pain, patient global, fatigue, anxiety, depression and quality of sleep, and demographic data including gender, age and formal education level. Physicians complete global assessment VAS, in addition to performing tender and swollen joint counts. RAPID3 (routine assessment of patient index data), DAS28 and CDAI are calculated. Demographics, self-reported disease activity measures, clinic data and medication usage were abstracted from the last visit of individuals with RA seen at three Turkish sites. Differences in measures were compared across sites and by status of biologic medication usage at last visit. Significant differences in measures were determined using the Kruskal-Wallis test for continuous and ordinal measures and Chi-square test for categorical measures.

**Results:** 140 RA patients were enrolled (mean age 54, disease duration 9.4 years, 79% female, education 7.5 years). Overall, 21% of patients were in remission or low disease activity as measured by RAPID3, with slightly increased percentages when DAS28 and CDAI were compared, but not all patients had all variables for DAS28 at each visit. 25% of patients were on biologic agents, with some variation in use among the different centers, which was also seen for MTX (overall 51%) and prednisone use (overall 50%) (Table *on the following page*), along with higher number of patients with lower disease activity. Patients on biologic agents (n=32) had significantly longer disease duration and worse function compared to patients (n=108) on only DMARDs, likely a reflection of the point biologics were considered for use in this population.

**Conclusion:** In this Turkish RA population, roughly a quarter of the patients were in remission or low disease activity, with a quarter on biologic agents, a higher number than most European countries. There were also some differences among treatment centers, which may reflect both the types of patients seen and different treatment approaches. These data present an initial look at the current treatment of RA and the utility of a routine care registry in Turkey and will be enhanced with additional patients and longer follow up.

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**Table (PP-08):** Comparison of FMF patients, controls, and the effect of colchicine treatment on various biomarkers related with atherosclerosis.

| | Cerrahpaşa | GATA | Marmara | Total | p |
|---|---|---|---|---|---|
| N | 24 | 44 | 72 | 140 | |
| Age (years) | 50.8 (13.1) | 54.2 (13.2) | 55.1 (13.2) | 54.0 (13.2) | 0.298 |
| Duration (years) | 9.8 (7.6) | 8.0 (5.6) | 10.2 (8.5) | 9.4 (7.5) | 0.561 |
| Education (years) | 7.7 (3.9) | 8.4 (5.2) | 6.8 (4.5) | 7.5 (4.7) | 0.398 |
| Female [N (%)] | 17 (71%) | 35 (80%) | 58 (81%) | 110 (79%) | 0.593 |
| Function [0-10] | 1.8 (2.2) | 1.9 (1.9) | 2.6 (2.2) | 2.2 (2.1) | 0.111 |
| Pain [0-10] | 4.2 (3.5) | 4.2 (2.6) | 4.9 (2.6) | 4.5 (2.8) | 0.317 |
| Global [0-10] | 4.3 (2.6) | 4.4 (2.4) | 4.6 (2.4) | 4.5 (2.4) | 0.781 |
| RAPID [0-30] | 10.3 (7.1) | 10.6 (5.7) | 12.2 (6.4) | 11.4 (6.3) | 0.176 |
| RAPID Categories | | | | | 0.679 |
| High | 11 (46%) | 16 (42%) | 33 (52%) | 60 (48%) | |
| Moderate | 6 (25%) | 14 (37%) | 19 (30%) | 39 (31%) | |
| Low | 2 (8%) | 5 (13%) | 3 (5%) | 10 (8%) | |
| Near remission | 5 (21%) | 3 (8%) | 9 (14%) | 17 (13%) | |
| Fatigue [0-10] | 5.7 (3.7) | 5.4 (3.2) | 4.4 (2.9) | 4.9 (3.2) | 0.146 |
| Swollen [0-28] | 1.8 (4.5) | 1.5 (3.4) | 1.5 (2.8) | 1.6 (3.3) | 0.724 |
| Tender [0-28] | 2.9 (6.6) | 5.2 (8.2) | 1.1 (3.0) | 2.7 (6.0) | 0.005 |
| MD Global [0-10] | 2.1 (2.2) | 3.1 (2.6) | 3.0 (1.4) | 2.8 (2.2) | 0.076 |
| ESR (mm/hr) | 38.7 (27.8) | 25.3 (15.4) | 23.1 (16.9) | 27.1 (19.9) | 0.032 |
| CRP (mg/dL) | 10.8 (12.9) | 10.3 (13.9) | 8.9 (10.4) | 9.8 (12.1) | 0.600 |
| DAS28 [0-10] | 3.6 (1.5) | 3.9 (1.6) | 3.1 (1.1) | 3.5 (1.4) | 0.152 |
| DAS28 Categories | | | | | 0.067 |
| High | 2 (10%) | 10 (29%) | 1 (3%) | 13 (14%) | |
| Moderate | 8 (40%) | 11 (32%) | 18 (45%) | 37 (39%) | |
| Low | 5 (25%) | 5 (15%) | 5 (13%) | 15 (16%) | |
| Remission | 5 (25%) | 8 (24%) | 16 (40%) | 29 (31%) | |
| CDAI [0-76] | 11.3 (12.8) | 14.7 (13.9) | 10.9 (6.5) | 12.6 (11.7) | 0.443 |
| CDAI Categories | | | | | 0.287 |
| High | 3 (14%) | 9 (24%) | 1 (4%) | 13 (15%) | |
| Moderate | 3 (14%) | 8 (22%) | 10 (36%) | 21 (24%) | |
| Low | 11 (50%) | 14 (41%) | 15 (54%) | 41 (47%) | |
| Remission | 5 (23%) | 5 (!4%) | 2 (7%) | 12 (14%) | |
| Prednisone [N (%)] | 20 (83%) | 22 (50%) | 28 (39%) | 70 (50%) | 0.001 |
| Methotrexate [N (%)] | 19 (79%) | 27 (61%) | 26 (36%) | 72 (51%) | <0.001 |
| Hydroxychloroquine [N (%)] | 2 (8%) | 10 (23%) | 13 (18%) | 25 (18%) | 0.367 |
| Leflunomide [N (%)] | 3 (13%) | 15 (34%) | 20 (28%) | 38 (27%) | 0.150 |
| Sulfasalazine [N (%)] | 2 (8%) | 6 (14%) | 17 (24%) | 25 (18%) | 0.188 |
| Adalimumab [N (%)] | 4 (17%) | 6 (14%) | 4 (6%) | 14 (10%) | 0.152 |
| Etanercept [N (%)] | 2 (8%) | 2 (5%) | 7 (10%) | 11 (8%) | 0.694 |
| Infliximab [N (%)] | 3 (13%) | 0 (0%) | 2 (3%) | 5 (4%) | 0.039 |
| Rituximab [N (%)] | 0 (0%) | 0 (0%) | 4 (6%) | 4 (3%) | 0.295 |

# Difficult Cases

## (DC-1 — DC-3)

### DC-1

### A male patient with systemic lupus erythematosus and proteinuria

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A 26 year old male was admitted to the department of Rheumatology because of peripheral edema and refractory proteinuria. His disease started when he was 21 years old. He was first admitted to hospital with acute onset of fever, chills, watery diarrhea, pain on urination and a pollakuria with a frequency of 20 times every day. Personal history was unremarkable. Father had rheumatoid arthritis and aunt had SLE. At his initial admission at the age of 21 years he had an overactive bladder with diffuse bladder wall thickening, bilateral hydronephrosis and increased trabeculation on cystoscopy. There was no evidence of retroperitoneal fibrosis. After two weeks, he developed an acute confusional state, hemolytic anemia with positive antiglobulin tests. ANA and anti DNA was positive, He tested positive for anticardiolipin antibodies and lupus anticuagulant. He had a proteinuria of 3 gr/day with few erythrocytes and leukocytes in the sediment with no casts. The renal biopsy showed no glomerulonephritis and no immune-depostion. He was treated with warfarin anti-coagulation, high dose corticosteroids and cyclophosphamide with improvement in the hemolysis and neurologic disease. Proteinuria decreased to 1.7 gr/day after 15 months. Treatment was switched to azathioprine 150 mg/day. After 1 year at age 23 he was readmitted with increased proteinuria (11.6 gr/day) and recurrence of lower urinary tract symptoms. His bladder was injected with botilinum toxin and his treatment was switched to mycophenolate mofetil 2gr/day. The proteinuria increased to 22 g/day in the following year, a rectal biopsy was negative for amyloid. He was switched to rituximab 1000 mg 2 infusions 14 days apart every 6 months. After 8 courses of rituximab the proteinuria was 13.5 gr/day. A new renal biopsy was done in 2011. The final diagnosis was focal segmental glomerulosclerosis.

### DC-2

### A Sjögren's syndrome patient with systemic manifestations

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Sjogren's syndrome (SS) can be fatal if it is associated with cryoglobulinemic vasculitis. The cause of poor prognosis can be due to disease itself or drugs used for its treatment. In this case report, we presented a case with SS who developed multi-organ involvement and fatal outcome. In Jan 2007, A-44-year old female was hospitalised in Neurology Department because of right drop foot. She had a history of Raynaud phenomenon for 10 years, dry mouth and dry eyes for 5 years. On laboratory examination, ANA, SS-A and SS-B antibodies were positive, minor salivary gland biopsy was concordant with SS. The ENMG showed diffuse sensorymotor peripheral neuropathy. Bilateral reticulonodular infiltration was seen in the chest X ray. HRCT revealed the presence of lymphocytic interstitial pneumonia. She was diagnosed as having Primary SS with neurologic and pulmonary involvement. Thorax and abdominopelvic CTs for the evaluation of lymphoma were found to be normal. She was treated with high dose steroids and cyclophosphamide. She went into remission. Two years later, cryoglobulinemic vasculitis with renal and pulmonary involvement were developed while she was on azathioprine. Cyclophosphamide and high dose steroid were re-admitted. Two months later pneumonia developed. After resolution of pneumonia with antibacterial and antifungal therapy, rituximab was started for resistant disease. Lymphoma work up was done again and all were negative once more. After the first dose of RTX she was in remission but then she was lost to follow up. Eight months later she died because of sepsis in the intensive care unit. Sjogren's Syndrome can be so resistant mostly when complicated with cryoglobulinemic vasculitis and may lead to fatal outcome.

### DC-3

### A patient with clinically amyopathic dermatomyositis and interstitial lung disease.

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A 32 year old femalewas admitted to the hospital with pain in all extremities, weight loss of 10 kg per month, malaise, alopecia, dyspnea on exertion, dry cough and rash on face and hands. She had no remarkable past or family history. Physical examination revealed erythematous face, periorbital edema and gottron-like papules around metacarpophalangeal and proximal interphalangeal joints. She had Raynaud's phenomenon. Laboratory tests revealed leukopenia, lymphopenia (WBC: 3,800 cells/ml, lymph: 800 cells/ml), mild CK, AST, ALT elevation (CK: 245 U/L, AST: 54 IU/L, ALT: 50 IU/L), poly-

clonal gammopathy (gammaglobulin 20.9%) without any acute phase response. She had negative ANA and ANCA and aldolase level was normal. Schirmer's test was 18 mm/min on both eyes with normal salivary gland biopsy. Although chest X-ray was normal, CT scan showed interstitial lung disease. An electromyography showed myogenic involvement in proximal muscles, she had a proximal muscle biopsy from a quadriceps. Interface dermatitis was observed in a skin biopsy taken from the lesions on the hands.She was treated with hydroxychloroquine(400 mg/day) and prednisolone(30 mg/day) with a diagnosis of undifferentiated connective tissue disease. In the second week of treatment muscle biopsy was back and showedmyocyte degeneration and inflammatory infiltrates in perimysial vessel walls which was interpretedas vasculitis. Therefore, 3 pulses of 1 gram methylprednisolone were given, daily prednisolone dose was increased to 60 mg/day and methotrexate 15 mg/weekwas added to the treatment and gradually increased to 25 mg/week in 3 weeks. On the sixth week of admission dyspnea worsened and she developed painful ulcers on both elbows and extensor surfaces of the hands over MCP joints, arthritis in MCPs, PIPs and knees with a tendon rupture in the left hand second extensor tendon. On physical examination, she had basal and mid-zone crackles in the lungs and gross nailfold capillary dilatations were detected. Because of severe respiratory symptoms, CT scan was repeated and showedsignificant progression in the interstitial infiltrates. In the tenth week of admission the treatment was switched to cyclophospamide 1 gm/monthandprednisolone 90 mg/day and another round of3-day pulsed methylprednisolone was givenwith no improvement. She then suffered aCMV infectionandwas followed in intensive care unit for two days because of respiratory insufficiency with noninvasive support. During follw-up CRP decreased and CMV-DNA became negative with antiviral treatment. An IVIG therapy was started aftewards and the paitent's functional status improved significantly, the ulcers healed and photosensitivity resolved. During the tratment she had positive ANA on the fourth time she was tested. Though tested for a number of antibodies of antisynthetase syndrome, all were negative. The patient is stil under monthly IVIG treatment. She now has no symptoms and the interstitial changes in the lungs have improved.