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Fifty shades of remission in RA**OP0192 ADDING ULTRASOUND TO THE TREAT-TO-TARGET STRATEGY SHOWS NO BENEFIT IN ACHIEVEMENT OF REMISSION: RESULTS FROM THE BIODAM COHORT**

A. Sepriano¹, S. Ramiro¹, R. Landewé², D. van der Heijde¹, S. Ohnrdorf³, O. FitzGerald⁴, M. Backhaus³, M. Larché⁵, J. Homik⁶, A. Saraux⁷, H. Hammer⁸, L. Terslev⁹, M. Østergaard¹⁰, G. Burmester³, B. Combe¹¹, M. Dougados¹², C. Hitchon¹³, G. Boire¹⁴, R. Dadashova¹⁵, J. Paschke¹⁵, E. Hutchings¹⁵, W. Maksymowych⁶. ¹LUMC, Leiden; ²ARC, Amsterdam, Netherlands; ³Charité, Berlin, Germany; ⁴SVUH, Dublin, Ireland; ⁵McMaster University, Hamilton; ⁶University of Alberta, Edmonton, Canada; ⁷CHU, Brest, France; ⁸Diakonhjemmet Hospital, Oslo, Norway; ⁹Copenhagen UH, Copenhagen; ¹⁰Copenhagen UH, Copenhagen, Denmark; ¹¹CHU, Montpellier; ¹²Descartes University, Paris, France; ¹³University of Manitoba, Winnipeg; ¹⁴University of Sherbrooke, Quebec; ¹⁵CaRE Arthritis Ltd, Edmonton, Canada

Background: While, a Treat-to-Target strategy (T2T), treating patients with rheumatoid arthritis (RA) towards a certain target (eg. clinical remission; T2T-REM), is highly recommended, several patients in clinical remission often have residual synovitis on ultrasound-imaging (US). This may result in silent radiographic progression and clinical flare. It is arguable whether targeting US-synovitis may result in "deeper" remission in clinical practice.

Objectives: To assess whether using US in a T2T strategy leads to more patients meeting clinical remission than using only clinical information.

Methods: Patients with RA who started or changed csDMARD and/or anti-TNF treatment followed in centers with expertise in US and participating in BIODAM (2-year multicenter prospective observational cohort) were included. Clinical and US data [by the US7-score that includes 7 joints of the clinically dominant hand and foot for synovitis and tenosynovitis on gray-scale US (GSUS) and power-doppler US (PDUS) and erosions on GSUS] were collected every 3 months. Per visit was decided whether the patient was treated according to the clinical definition of T2T with remission as benchmark (T2T-CLIN-REM). Though not mandatory, US-data could also be used for this purpose. T2T-CLIN-REM was considered correctly applied if: either i) a patient already had a disease activity score below the remission target (i.e. ACR/EULAR boolean remission) or ii) if not, treatment was intensified. A T2T strategy taking also US data into account (T2T-CLIN-US-REM) was considered correctly applied if: either i) both clinical and US remission (all joints included in the US7-score with GSUS synovitis <2 and PDUS synovitis=0) were present; or ii) if not, the treatment was intensified. The main outcome was ACR/EULAR boolean remission. The effect of adding US to T2T (T2T-CLIN-US-REM) on clinical remission 3 months later compared to a clinical remission benchmark only (T2T-CLIN-REM) was analyzed using generalized estimating equations with auto-regression.

Results: In total 963 visits of 130 patients were included. T2T-CLIN-US-REM was correctly followed in 33% of the visits, T2T-CLIN-REM in 14%, and any of these in 52%. Remission according to the ACR/EULAR-boolean definition was achieved in 19.6% of the visits. Compared to the conventional T2T-CLIN-REM strategy, using a combined clinical and US benchmark for T2T led to a lower – instead of higher – likelihood of ACR/EULAR-boolean remission 3 months later [OR (95% CI): 0.39 (0.24; 0.63) (table)].

Table. Effect of following a T2T strategy taking both clinical and US data into account (T2T-CLIN-US-REM) compared to the clinical definition of T2T (T2T-CLIN-REM; reference) in meeting the targets 3 months later and over a period of 2 years.

T2T approach	Outcome	ACR/EULAR boolean remission
		aOR* (95% CI)
No T2T vs T2T-CLIN-REM alone [§]		0.49 (0.27; 0.88)
T2T-CLIN-US-REM vs T2T-CLIN-REM alone [§]		0.39 (0.24; 0.63)

*Adjusted for age, gender, HAQ-score, RF, ACPA, previous use of DMARDs, smoking-status, education and number of comorbidities. § Clinical definition of T2T (T2T-CLIN-REM) was used as the comparator for each of the presented treatment strategies.

Conclusions: Our results, from a non-randomized study, did not suggest an advantage of using US of 7 joints in addition to clinical examination as a T2T benchmark as compared to clinical examination alone in getting RA patients into clinical remission.

Disclosure of Interest: None declared

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Innate immunity**OP0193 INFLAMMATION OF ADVENTITIAL NERVES OCCURS IN GIANT CELL ARTERITIS PATIENTS AND IT IS CHARACTERIZED BY INFLAMMASOMES, UPR AND AUTOPHAGY ACTIVATION**

F. Ciccio¹, A. Rizzo¹, R. Alessandro¹, S. Raimondo¹, G. Guggino¹, A. Cavazza², C. Salvarani², G. Triolo¹. ¹University of Palermo, Palermo; ²Arcispedale Santa Maria Nuova, Reggio Emilia, Italy

Background: Vascular adventitia is a major site of immune surveillance and inflammatory cell trafficking and is the most complex compartment of the vessel wall comprising fibroblasts, dendritic cells and macrophages, progenitor cells, vasa vasorum, pericytes and adrenergic nerves. It has been proposed that activation of adventitial nerves and release of sensory neuropeptides from their peripheral terminals may lead to neurogenic inflammation. Giant cell arteritis (GCA) is an immune-mediated disease of unknown etiology in which the inflammatory process seems to start from the adventitia of affected arteries.

Objectives: aim of the study was to evaluate the occurrence of adventitial nerves inflammation and to immunologically characterize the adventitial neuritis occurring in GCA patients.

Methods: Immunohistochemistry and RT-PCR were used to study the presence of neuritis in temporal artery samples obtained from 30 patients with temporal artery (TAB) positive GCA, 20 TAB negative GCA and 20 controls. Laser capture microdissection (LCM) was used to isolate adventitial nerves and nerve expression of pro-inflammatory cytokines involved in the pathogenesis of GCA such as IL-6, IL-17, IL-32, IL-9, IL-33 was assessed by RT-PCR. Expression of pro-inflammatory cytokines by adventitial nerves was further studied by immunohistochemistry and confocal microscopy. Autophagy, unfolded protein response (UPR) and inflammasomes pathways were also studied by RT-PCR and immunohistochemistry.

Results: Adventitial nerves showed infiltration of CD3⁺ T cells in all the TAB positive and in 12 out of 20 TAB negative arteries but were never observed in control arteries. RT-PCR expression analysis of different pro-inflammatory cytokines clearly demonstrated specific over-expression of IL-33 in LCM isolated inflamed nerves. Immunohistochemical and confocal microscopy analysis confirmed nerve IL-33 expression. RT-PCR and immunohistochemistry demonstrated that AIM2 and NLRP3, but not NLR4, inflammasomes were activated in inflamed nerves of GCA patients. According to inflammasomes activation, increased IL-18 expression was observed. Autophagy-related genes such as ATG16L1 and LC3 and UPR-related genes such as XBP-1 and CHOP were also over-expressed in GCA adventitial nerves as demonstrated by RT-PCR and immunohistochemistry. Finally, increased expression of AIM2 and NLRP3 inflammasomes, autophagy and UPR was also observed outside the nerves, in the context of inflamed artery wall.

Conclusions: here we demonstrated that adventitial neuritis is present in both inflamed and non-inflamed arteries of GCA patients. GCA inflamed nerves specifically produce IL-33 a cytokine of the innate immunity that has been demonstrated to be involved in the pathogenesis of GCA. AIM2 and NLRP3 inflammasomes activation was also observed in GCA arteries and in particular in the inflamed adventitial nerves being accompanied by the increased expression of IL-18. Specific activation of autophagy and UPR pathways was also observed in the inflamed GCA nerves. Altogether these findings seem to suggest a complex immune activation of adventitial nerves in GCA, suggesting a possible role of arterial neuritis in the initiation and perpetuation of GCA artery inflammation.

Disclosure of Interest: None declared

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OP0194 INVOLVEMENT OF TOLL-LIKE RECEPTOR 9 IN THE PATHOGENESIS OF EROSIVE AUTOIMMUNE ARTHRITIS AND DURING OSTEOCLASTOGENESIS

A. Fischer, B. Meyer, B. Niederreiter, G. Steiner. *Internal Medicine III-Rheumatology, Medical University Vienna, Vienna, Austria*

Background: Release and insufficient removal of endogenous nucleic acids may be involved in triggering harmful autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 7 and 9, have been linked to pathogenic autoimmune processes, particularly in systemic lupus erythematosus, but their role in RA is less clear. Results previously obtained in rats with pristane-induced arthritis (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model (1). Interestingly, rats with PIA develop autoantibodies associated with RA including rheumatoid factor, anti-RA33 and antibodies to carbamylated proteins (2).

Objectives: To gain more insight into the role of TLR9 in the pathogenesis of autoimmune arthritis by investigating the effects of TLR9 inhibition in rats with PIA.

Methods: Arthritis was induced in DA rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist every other day, starting one before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Expression of TLR9

and other nucleic acid sensing TLRs was quantified by RT-PCR and Western blotting; activation (phosphorylation) of various signal transduction molecules was determined by Western blotting. Furthermore, the role of TLR9 in osteoclast differentiation and activation was investigated *in vitro*.

Results: The TLR9 antagonist significantly reduced clinical signs of arthritis by approximately 50%. Histological analyses revealed diminished inflammation, cartilage degradation, bone erosion and significantly reduced numbers of osteoclasts in animals treated with the TLR9 antagonist. However, when treatment was started after onset of arthritis TLR9 inhibition had no effect on arthritis development and severity. IL-6 serum levels were greatly diminished in animals treated with the TLR9 antagonist and expression and activation of NF- κ B in lymph nodes was reduced. Remarkably, mRNA levels of TLR7 and TLR9 strongly differed in the course of *in vitro* osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and stimulation with a TLR9 agonist (CpG) completely inhibited osteoclastogenesis.

Conclusions: Taken together, the results suggest an important role for TLR9 in the T cell-dependent initiation phase of PIA and thus important involvement of endogenous DNA released during apoptosis, necrosis or netosis in the initiation of autoimmune arthritis and during osteoclastogenesis. The possible relevance of these findings for human RA needs to be further elucidated in future experiments.

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To be and to become: transition from paediatric to adult care

OP0195 WHAT IS THE IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD? THE MONOCENTRIC EXPERIENCE OF 240 PATIENTS FOLLOWED IN A TRANSITION TERTIARY CLINIC OF RHEUMATOLOGY

I. Pontikaki¹, L.M. Argolini², C. Artusi², P.L. Meroni³. ¹Unit of Pediatric Rheumatology-Department of Rheumatology; ²Department of Rheumatology; ³Department of Rheumatology, Chair of Rheumatology, Gaetano Pini Institute, University of Milan, Milan, Italy

Background: There are many differences in clinical manifestations, assessment and management of Juvenile Idiopathic Arthritis (JIA) between childhood and adults' arthritis onset. The transition from pediatric to the adult care emphasizes a lot of aspects that need to be addressed.

Objectives: To describe the long-term outcome of JIA.

Methods: Two-hundred and forty patients affected by JIA and referred to a transition care rheumatology tertiary centre were considered between 1999 and 2016. The outcome assessment included disease activity, medications, number of prosthesis implantation, pregnancy, mortality, social integration (mobility, employment status and educational level).

Results: Seventy-four (30.8%) males and 166 (69.2%) females were included; 53 (22.1%) patients were lost in follow up. Subtypes of JIA at disease onset included 101 oligoarthritis (42.1%), 67 polyarthritis (27.9%), 43 systemic arthritis (17.9%),

7 psoriatic arthritis (2.9%), 22 enthesitis related arthritis (9.2%). Forty-eight (20%) patients had persistent uveitis. Ninety-three implant prosthesis and 14 arthrodesis were recorded. The average disease duration was 20 years, the median age of the patients was 27 (18–57) years. Five deaths (2.1%) occurred in this cohort. At follow up 117 (48.7%) had low active disease activity, 70 (29.2%) had moderate disease activity, 14 (5.8%) had a high disease activity, 24 (10%) were on remission ON medication and 15 (6.3%) OFF medication. Among patients still on medication, 59 (24.6%) were treated with oral steroids, 18 (7.5%) with csDMARDs and 169 (70.4%) with bDMARDs. Seventy-five (31.3%) patients had a higher educational level (university), 195 (81.3%) had an employment, 128 (53.3%) had a driving license. Twenty-one (8.8%) pregnancies were registered. The transition age was considered after age of sixteen years old. In this context, it was important the multidisciplinary approach of each patient that was realized with the collaboration of other specialists (ophthalmologist, orthopedic, dermatologist, obstetric, psychologist).

Conclusions: In the era of biologic therapy there was an important improvement in a lot variables of the long-term outcome of JIA. One-hundred-eighty-seven (77.9%) patients were still in tight control, not only because of the continuation of the biological therapy but also because of the multidisciplinary care carried out even during remission. JIA often persists over the adulthood. The long term follow up and care of these patients has to be conducted by a rheumatologist expertized in JIA in collaboration with other specialists.

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Heterogeneity in JIA

OP0196 CHANGING PATTERNS OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS TREATED WITH ETANERCEPT FROM 2000 TO 2016 IN THE GERMAN BIKER REGISTRY POPULATION

G. Horneff¹, K. Minden², I. Foeldvari³, G. Ganser⁴, J.P. Haas⁵, J. Brunner⁶, I. Becker⁷ on behalf of BIKER collaborative group. ¹Paediatrics, Asklepios, Sankt Augustin; ²Charité, Berlin; ³Private office, Hamburg; ⁴Ped Rheumatol, Sendenhorst; ⁵German Ped Rheum Centre, Garmisch-Partenkirchen, Germany; ⁶University, Innsbruck, Austria; ⁷University, Cologne, Germany

Background: There is increasing experience with Etanercept (ETA) in juvenile idiopathic arthritis in the BIKER Registry.

Objectives: To report on practice changes ETA utilization and outcome over a period of 16 years.

Methods: 6 cohorts of pts were created according to inclusion period. Patients' and disease characteristics, the utilization of DMARDs, steroids, NSAIDs were analysed. Efficacy was judged by PedACR30/50/70/90, JADAS and ACR-remission.

Results: Records from 2105 JIA pts treated with etanercept with at least a baseline and one follow up form were analysed. Most pts were females (67%). The median age of disease onset increased from 5.9 years in the early to 9.3 years in the later cohorts while age at start of treatment remained stable (about 13 years). Median disease duration markedly decreased from 5.3 to about 2 years. Most pts had RF neg. polyJIA followed by extended oligoarthritis. In the more recent cohorts the rate of enthesitis related arthritis increased and the rate of systemic JIA decreased (table). At registry start, 20% of newly enrolled pts belonged to the systemic JIA category compared to <1% in 2016. During the study period, the overall utilization of glucocorticoids at baseline decreased from 54% to 19% ($P<0.0001$), NSAID from 90% to 72% ($P<0.0001$), MTX from 78% to 64% ($P=0.004$). ACR30/50/70/90 response rates at month 12 were 80%/74%/59%/40% and did not vary over time while the rate of patients reaching no active joint/CHAQ DI=0/JADAS-MDA/JADAS-Remission/ACR-Remission increased from 43%/35%/44%/19%/41% to 69%/48%/45%/26%/63%.

Abstract OP0196 – Table 1

Year	2000–2002 N=248	2003–2005 N=337	2006–2008 N=444	2009–2011 N=462	2012–2014 N=436	2015–2016 N=178
Disease duration (y)	6.1±4.0	5.1±4.0	4.2±3.7	3.7±3.0	3.3±3.1	3.4±3.0
JIA category (%)						
Sys JIA	20.6	12.2	4.3	3	1.4	0.6
RFneg PA	25.8	31.8	32.9	36.6	33	33.7
RFpos PA	12.5	11.0	8.1	8	3.7	9.0
PersOA	2.4	4.5	6.1	6.1	3.4	5.1
Ext OA	18.1	13.1	21.4	22.3	21.3	21.9
ERA	9.7	14.7	16.4	13.6	26.1	22.5
PsA unclass JIA	4.8	8.9	7.7	7.8	8	4.5
Uveitis	6	3.6	3.2	2.6	3	2.8
Baseline concom. NSAID/steroids/MTX/other DMARDS (%)	12.1	5.7	10.2	5.4	4.1	2.3
Active joints	90.3/53.2/77.8/5.2	88.7/42.7/76.3/5	84.9/32.4/69.1/3.8	71.31/68.4/3.7	78.7/27.3/61/6.7	74.2/18.5/62.9/4.5
Phy VAS (0–10)	10.3±9.8	9.0±9.4	7.8±9.0	6.2±8.0	4.9±6.5	4.6±5.5
Pat VAS (0–10)	6.8±2.4	5.8±2.6	5.2±2.6	4.9±2.9	5.0±2.6	4.8±2.5
CHAQ	5.7±2.7	5.4±2.7	4.8±2.6	3.7±2.7	3.7±2.6	3.7±2.3
CRP in mg/l	1.0±0.8	0.8±0.7	0.7±0.6	0.6±0.6	0.5±0.6	0.5±0.5
JADAS10	44.6±56.8	25.2±32.2	18.2±32.1	10.6±19.1	9.8±29.1	8.9±18.1
JADAS10	21.4±7.7	18.5±7.5	16.6±6.7	14.1±8.7	13.3±6.8	13.3±8.7

Changes in all parameters were significant ($p<0.001$) in Kruskal-Wallis-Test/Chi-square.