(CRP)-level, visual analogue scale of disease activity and pain, disease activity score, psoriasis area severity index (PASI)-score), disease effects (total Sharp score, health assessment questionnaire disability index (HAQ-DI)-score) and prior treatments. For the continuous data, we calculated a weighted mean and standard deviation (SD) per period. Data not available in the form of mean ±SD in the original studies were therefore not included. For the discrete data, we summed up the patients meeting the criterium from all the studies in a given period and calculated a percentage. We used the RStudio software. For the normally divided data, we used ANOVA-test for a group analysis to find significant differences between the time periods. For the discrete data, we used Chi-square test.

Results: Detailed analysis of the baseline characteristics showed some remarkable differences between the three different treatment periods with most data indicating that these shifts have occurred between the first and the second period. In comparison to the initial trials with etanercept, infliximab and adalimumab, gender and race show more diversity, patients are older but have a shorter disease duration, show lower swollen and tender joint counts, but more enthesitis, and have lower CRP-levels. Although several of these parameters suggest an overall lower disease activity in the second and third period of trials, this is not reflected in the physician's and patient's perspective of disease activity and the HAQ-DI score.

Conclusions: Our analysis found significant differences in patient characteristics, disease characteristics, disease activity, disease effects and use of prior treatments between the 3 periods of treatment drugs since the introduction of biologicals. Patients appear to be considered earlier and with less severe disease albeit that the subjective evaluation of disease activity goes in the opposite direction.

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OP0312

INTERNATIONAL LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (ILAR) TREATMENT RECOMMENDATIONS FOR PSORIATIC ARTHRITIS IN RESOURCE-POOR COUNTRIES

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Background: The European League Against Rheumatism (EULAR) and the Group for Research and Assessment of Psoriasis and PsA (GRAPPA) updated their respective recommendations for the management of PsA in 2015. However, these guidelines are primarily based on studies conducted in resource replete countries; hence they may not be applicable to countries in Central and South America, and Africa. Therefore, new ILAR recommendations have been developed for these regions adapted from existing recommendations.

Objectives: To establish ILAR recommendations for the management of PsA in resource poor settings, particularly Central/South America and Africa, using an expert local panel, adaptation of existing EULAR and GRAPPA treatment recommendations and a new systematic literature review (SLR) for specific issues in resource-poor countries.

Methods: The ADAPTE Collaboration process[1] for guideline adaptation was followed to assess and adapt the EULAR and GRAPPA treatment recommendations for PsA covering the Americas and Africa. The process was conducted according to its three phases: set-up phase (identifying and seeing agreement from a panel of participants from the relevant countries), adaptation phase (defining health questions using the PIPOH tool, assessing the two source recommendations, conducting an SLR to answer health questions not addressed in the two source recommendations, assessing quality of source recommendations, assessing applicability of principles contained in the source recommendations, and drafting adapted recommendations), and finalisation phase (external review, aftercare planning and final production).

Results: Five principles for the management of PsA were developed addressing 1. Goals of therapy, 2. Assessment of domains, 3. Assessment of relevant comorbidities, 4. Safety of pharmacotherapy and shared decision making, and 5. Frequency of follow up. Six recommendations for the management of PsA were also developed addressing 1. Goals of therapy, 2. Screening and management of tuberculosis, HIV, HBV, HCV, Chagas' disease, leishmaniasis, leprosy, and other concomitant comorbidities, 3. Frequency of monitoring in resource poor countries, 4. Safety and efficacy of pharmacotherapy in all domains, 5. Efficacy and safety of combination therapy, and 6. Safety and efficacy of biosimilars and intended copies.

Conclusions: ILAR recommendations for the management of PsA in resource-poor countries are now available, developed by adapting principally the GRAPPA recommendations, but also the EULAR recommendations, supplemented by expert opinion from these regions.

REFERENCE:

[1] The ADAPTE Collaboration. The ADAPTE Process: Resource Toolkit for Guideline Adaptation, *Version 2.0* 2009. [Available from] http://wwwg-i-n.net

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T/B be or not T/B: adaptive or innate immunity – that is the question

OP0313

MOLECULAR ANALYSIS OF ANTI-CITRULLINATED PROTEIN ANTIBODY VARIABLE REGIONS INDICATES ABERRANT SELECTION PROCESSES DURING ACPA B-CELL DEVELOPMENT

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Background: Anti-citrullinated protein antibodies (ACPA) represent the most specific biomarker in Rheumatoid Arthritis (RA) and have been associated with RA pathogenesis. ACPA-IgG are heavily *N*-glycosylated in the variable domain. Recently, we showed that>80% of ACPA-IgG clones harbour *N*-glycosylation sites in their variable regions that result from somatic hypermutation (SHM). The reason for this remarkable phenomenon is incompletely understood. Elucidation of its molecular basis might provide insights into mechanisms by which ACPA-expressing B cells breach tolerance.

Objectives: To understand the molecular origin of ACPA variable domain *N*-glycosylation based on B-cell receptor (BCR) sequence analyses.

Methods: ACPA-expressing B cells were isolated from peripheral blood of 12 ACPA-positive RA patients using CCP2-streptavidin tetramers and fluorescence activated cell sorting. Full-length immunoglobulin (Ig) transcripts of heavy chains (HC) and light chains (LC) were obtained using anchoring reverse transcription of Ig sequences and amplification by nested PCR. Sequences were analysed for the degree of SHM and the presence of *N*-glycosylation sites (defined as sequences encoding N-X-S/T (X $\neq$ Proline) in the protein backbone). Sites that required a single nucleotide mutation to be generated were defined as s-SHM sites, whereas sites requiring multiple mutations were defined as m-SHM sites. IgG sequences of 12 healthy donors were used as control.

Results: 67% of ACPA-Igκ LC and 47% of ACPA-Igλ LC contained $\geq$1 n-glycosylation sites compared to 82% of ACPA-IgG HC. Nucleotide mutation rates were similar for ACPA-Igκ LC and ACPA-Igλ LC (88.2%±5.7% and 87.3%±5.3% similar to germline, respectively) and lower compared to the mutation rate of ACPA-IgG HC (82.4%±5.8% similar to germline). The distribution of sites in ACPA-Igκ LC and ACPA-IgG HC was similar, with most sites located in framework region (FR) 3 (42% and 49%, respectively). In contrast, 65% of all *N*-glycosylation sites in ACPA-Igλ LC clones were located in FR1 and only 7% were located in FR3.
Furthermore, 26% of all *N*-glycosylation sites in ACPA-IgG HC were m-SHM sites compared to 15% in IGHV-matched IgG clones derived from healthy donors. 28% and 44% of all *N*-glycosylation sites were m-SHM sites in ACPA-Igκ LC and ACPA-Igλ LC, respectively. No correlation was observed between the number of nucleotide mutations and the number of total *N*-glycosylation or m-SHM sites in ACPA clones.

Conclusions: Our analyses revealed an abundance of *N*-glycosylation sites in ACPA-IgG HC, ACPA-Igκ LC and ACPA-Igλ LC. *N*-glycosylation sites in ACPA are frequently m-SHM sites. Intriguingly, the generation of such sites requires multiple somatic mutations suggesting that m-SHM sites in specific positions in ACPA variable regions could be advantageous for the survival of ACPA-expressing B cells. This indicates that the introduction of *N*-glycosylation sites might be a selective process that could allow these B cells to escape from putative tolerance checkpoints.

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