patients achieving PASI-75/PASI-50 among those with dactylitis or enthesis at baseline. Safety is described for the overall PALACE 1-3 population.

**Conclusions:** ACR20/60/70 receiving APR30 demonstrated significant improvements in core PsA domains. The data may explain why patients who failed to achieve an ACR20 response remained on long-term APR treatment. The findings suggest that some subjects with PsA may experience meaningful clinical improvement that is not completely captured by the assessment of ACR20 response criteria. Outcome measures specifically designed for PsA subjects may be more suitable to evaluate treatment response in PsA subjects.

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**OP0311 NOTABLE EVOLUTIONS IN THE CHARACTERISTICS OF PsA PATIENTS FROM CLINICAL TRIALS POPULATIONS IN THE ERA OF BIOLOGICAL TREATMENTS**


**Background:** Psoriatic arthritis is a chronic inflammatory disease that affects the musculoskeletal system. It can include arthritis, spondylitis, dactylitis and enthesis, and is strongly associated with the presence of psoriasis. The introduction of biological therapies as a treatment option has brought a significant improvement in disease control for these patients.

**Objectives:** In this study, we wanted to detect emerging differences in demographic and clinical characteristics of the PsA-patient study population since the introduction of biologicals.

**Methods:** We selected 12 phase II- and phase III-trials and divided them into 3 treatment periods based on different time windows and working mechanisms of the particular biologics or targeted DMARDs. Published tables with the baseline demographic and clinical characteristics of study population from the individual studies were used. For inclusion of a specific parameter, it had to be present in at least one study of each period. An exception to this rule was made for the ‘number of patients with prior anti-TNF therapy’, only present in studies from the second and third period. Parameters were defined in different categories: patient characteristics (gender, age, race, weight), disease characteristics (duration of PsA, presence of dactylitis, presence of enthesis, psoriasis body surface area), disease activity parameters (swollen joint count, tender joint count, C-reactive protein level), and other disease activity parameters like use of concomitant non-steroidal anti-inflammatory drugs.

**Conclusions:** Type 2 diabetes mellitus, hyperuricemia, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction and brain stroke event were more prevalent in men than in women with PsA. Male gender had correlation with the prevalence of cardiovascular events or their risk factors.

**REFERENCE:**


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INTERNATIONAL LEAGUE OF ASSOCIATIONS FOR MOLECULAR ANALYSIS OF ANTI-CITRULLINATED PROTEIN ANTIBODIES (ILAR) TREATMENT RECOMMENDATIONS FOR PSORIATIC ARTHRITIS IN RESOURCE-POOR COUNTRIES


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 process1 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 selecting agreement from a panel of participants from the relevant countries), adoption 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, 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. Efficacy 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.

Disclosure of Interest: None declared


Friday, 15 June 2018

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 ACPS 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 ACPS-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 ≠ 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-IgG LC and 47% of ACPA-IgG HC contained 1 N-glycosylation sites compared to 82% of ACPA-IgG HC. N-glycosylation site mutation rates were similar for ACPA-IgG LC and ACPA-IgG HC (82.4%±5.8% similar to germline). The distribution of sites in ACPA-IgG HC and ACPA-IgG LC 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-IgG LC 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-IgG LC and ACPA-IgG 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-IgG LC and ACPA-IgG LC. N-glycosylation sites in ACPA-IgG LC 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.

Disclosure of Interest: None declared

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OP0312

ABERRANT SELECTION PROCESSES DURING ACPS B-CELL DEVELOPMENT


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 process1 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 selecting agreement from a panel of participants from the relevant countries), adoption 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, 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