subjects achieving PASI-75/PASI-50 among those with psoriasis involvement $\geq 3\%$ of the body surface area at baseline, and dactylitis count and MASEs of 0 among those with dactylitis or enthesitis at baseline. Safety is described for the overall PALACE 1–3 population.

Results: A total of 109 subjects randomised to APR30 treatment at baseline were ACR20NRs at Week 104. Baseline ACR core components were similar for ACR20NRs and ACR20 responders at Week 104. Among these ACR20NRs, several core components of ACR response, including swollen/tender joint counts and Physician's Global Assessment of Disease Activity (visual analogue scale) scores, showed sustained improvements from baseline through Week 104 (table 1). Importantly, of the 109 ACR20NRs at Week 104, 50.0% achieved a PASI-50 response after continued treatment with APR30 through Week 104 (table 1). Among ACR20NRs with baseline dactylitis ($n=44$) or enthesitis ($n=74$), 68.2% achieved a dactylitis count of 0 and 33.8% achieved a MASEs of 0 at Week 104. More limited improvements in Subject's Global Assessment of Disease Activity, Subject's Assessment of Pain, Health Assessment Questionnaire-Disability Index, and C-reactive protein outcomes most commonly had an impact on subjects' ability to achieve an ACR20 response. In the overall subject population, no new safety concerns were identified through 104 weeks.

Abstract OP0309 – Table 1

	ACR20NRs at Week 104 With APR30 From Baseline ($n=109$)		
	Week 24	Week 52	Week 104
Swollen joint count (0–76), mean and median % change	-52.2, -71.4	-62.8, -73.3	-58.0, -75.0
Tender joint count (0–78), mean and median % change	-32.5, -47.4	-45.8, -53.5	-41.7, -51.7
PhGA (VAS 0–100 mm), mean and median % change	-37.9, -43.6	-49.8, -54.2	-44.3, -48.7
Dactylitis=0, n/m (%) ^a	23/44 (52.3)	29/44 (65.9)	30/44 (68.2)
MASEs=0, n/m (%) ^b	20/74 (27.0)	27/74 (36.5)	25/74 (33.8)
PASI-75, n/m (%) ^c	17/50 (34.0)	22/50 (44.0)	18/50 (36.0)
PASI-50, n/m (%) ^d	31/50 (62.0)	33/50 (66.0)	25/50 (50.0)

Data are as observed at Week 24, Week 52, and Week 104 for all subjects who were randomized to APR30 at baseline and were ACR20NRs at Week 104 and with a value at the time point indicated.
^aExamined among subjects with dactylitis at baseline. ^bExamined among subjects with enthesitis at baseline. ^cExamined among subjects with $\geq 3\%$ psoriasis involvement of the body surface area at baseline. PhGA=Physician's Global Assessment of Disease Activity; VAS=visual analog scale; n/m=number of subjects achieving response/number of subjects with evaluable data at the time point; MASEs=Maastricht Ankylosing Spondylitis Enthesitis Score; PASI-75/50= $\geq 75\%/ \geq 50\%$ reduction from baseline Psoriasis Area and Severity Index score.

Conclusions: ACR20NRs receiving APR30 demonstrated significant improvements in core PsA domains. The data may explain why subjects who failed to achieve an ACR20 response remained on long-term APR treatment. These 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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OP0310 PREVALENCE OF RISK FACTORS AND CARDIOVASCULAR EVENTS ACROSS PSORIATIC ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL THERAPY

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Background: Psoriasis and psoriatic arthritis (PsA) are described as associated with more frequency of risk factors and cardiovascular events.

Objectives: To determine the prevalence of risk factors and cardiovascular events in a cohort of patients with PsA treated with biological therapy and its correlation with gender.

Methods: We included all PsA patients (met CASPAR criteria) following treatment with bDMARDs (reference population 2.055.000). We obtained data of high

blood pressure, hyperlipidemia, hyperuricemia, type 2 diabetes mellitus, obesity (BMI ≥ 30), non-infectious liver disease, ischaemic cardiopathy, myocardial infarction, ischaemic stroke or transient ischaemic attack. For this analysis included gender, age, disease duration, current bDMARDs with or without current co-medication with csDMARDs and HLA-B27 status. Continuous variables were reported as mean $\pm$ standard deviation. Categorical variables were reported as percentages and frequencies. All analyses were performed using SPSS software. Differences were considered statistically significant if $p < 0.05$ (two-tailed).

Results: Data were obtained from 598 PsA patients who have been treated with bDMARDs. Three-hundred and twenty-five (54.3%) patients were men, mean age was 53.3 ± 12.6 years (men 53.3 ± 12.9 and women 53.2 ± 12.3 , $p=0.943$) and disease duration of PsA was 12.4 ± 8.7 years. No differences were seen for disease duration of PsA, nail disease, dactylitis, uveitis or HLA-B27. The prevalence of high blood pressure, hyperlipidemia, hyperuricemia, type 2 diabetes mellitus, obesity, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction (MI) and ischaemic stroke/transient ischaemic attack (IS) was 36.0%, 43.6%, 16.0%, 12.5%, 26.3%, 12.5%, 5.5%, 3.8% and 1.3%, respectively. Men had most prevalence of type 2 diabetes mellitus, hyperuricemia, non-infectious liver disease, ischaemic cardiopathy, myocardial infarction and brain stroke event (see table 1). Patients with MI or IS had more prevalence of CV risk factors.

Abstract OP0310 – Table 1

	Female (273)	Male (325)	P
High blood pressure, n(%)	98 (35.9)	117 (36.0)	0.979
Hyperlipidemia, n(%)	111 (40.7)	150 (46.2)	0.177
Hyperuricemia, n(%)	13 (4.8)	82 (25.3)	<0.001
Diabetes mellitus, n(%)	21 (7.7)	54 (16.6)	0.001
Liver disease, n(%)	19 (7.6)	49 (16.7)	0.002
Ischaemic cardiopathy, n (%)	8 (2.9)	25 (7.7)	0.011
Myocardial infarction, n (%)	5 (1.8)	18 (5.5)	0.019
Brain stroke event, n (%)	1 (0.2)	7 (2.2)	0.058

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.

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OP0311 NOTABLE EVOLUTIONS IN THE CHARACTERISTICS OF PSORIATIC ARTHRITIS CLINICAL TRIALS POPULATIONS IN THE ERA OF BIOLOGICAL TREATMENTS

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Background: Psoriatic arthritis is a chronic inflammatory disease that affects the musculoskeletal system. It can include arthritis, spondylitis, dactylitis and enthesitis, 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 biologicals 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 enthesitis, psoriasis body surface area), disease activity parameters (swollen joint count, tender joint count, C-reactive protein

(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 $\pm$ SD in the original studies were therefore not included. For the discrete data, we summed up the patients meeting the criterion 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 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 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.

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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-Ig κ LC and 47% of ACPA-Ig λ LC contained ≥ 1 n-glycosylation sites compared to 82% of ACPA-IgG HC. Nucleotide mutation rates were similar for ACPA-Ig κ LC and ACPA-Ig λ LC (88.2% $\pm$ 5.7% and 87.3% $\pm$ 5.3% similar to germline, respectively) and lower compared to the mutation rate of ACPA-IgG HC (82.4% $\pm$ 5.8% similar to germline). The distribution of sites in ACPA-Ig κ 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-Ig λ 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-Ig κ LC and ACPA-Ig λ 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-Ig κ LC and ACPA-Ig λ 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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