OP0038

HIGH PREVALENCE OF SACROILIAC BONE MARROW EDEMA ON MRI IN POSTPARTUM WOMEN: A TEMPORARY PHENOMENON

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Background: Magnetic Resonance Imaging (MRI) is a sensitive method for detection of sacroiliitis. However, recently, concerns have been raised about its specificity. In contrast to radiographic spondyloarthritis (SpA), non-radiographic SpA has a more equal sex distribution. Hence, in young women with back pain a broad differential diagnosis has to be considered. In clinical practice, women occasionally present with inflammatory(-like) low back pain, following pregnancy and childbirth. Up until now, little is known regarding the presence of SpA-like MRI lesions in postpartum women. We hypothesized that physical stress on the pelvis during pregnancy may lead to signs of bone marrow edema on MRI.

Objectives: To explore (A) the association between pregnancy and giving birth on the one hand, and the occurrence of MRI lesions compatible with SpA on the other hand; and (B) if these lesions are transient.

Methods: Twenty-five women underwent an MRI of the sacroiliac joints (SIJ) in the first 10 days after vaginal delivery. The scan was repeated after 6 months. Both time points were scored in pairs by 3 trained readers, blinded for time sequence and subject characteristics. MRI assessment was done on 6 consecutive slices for inflammatory and structural SpA-like lesions: bone marrow edema (BME), capsulitis, enthesitis, high signal intensity in joint space, erosions, fatty lesions, sclerosis and (partial) ankylosis. In addition, the Assessment of SpondyloArthritis International Society (ASAS) definition of a positive MRI-SIJ was applied. MRI reader scores were reported as 2 out of 3 (median) scores.

Results: Twenty out of 25 (80.0%) subjects displayed BME; the median SPARCC score was 5 (IQR 1-11) (see table). One subject was lost to follow-up. After 6 months, 11 out of 24 (45.8%) subjects still showed BME; however, median SPARCC score dropped to 0 (IQR 0-1) ($p = 0.002$). At baseline, 16 out of 25 (64.0%) participants had a positive MRI-SIJ according to the ASAS definition, reducing to 4 out of 24 (16.7%) after 6 months ($p = 0.002$). 75.5% of the baseline lesions were located in the anterior part of the SIJ; 57.3% situated on the iliac side. Structural lesions were rarely detected in this study population (see table).

Table: Number of MRI-SIJ lesions in 25 postpartum women.

	Baseline			6 months		
	Median	IQR	95% CI	Median	IQR	95% CI
Inflammatory lesions						
SPARCC (/72)	5	1 – 11	1 – 8	0	0 – 1	0 – 1
Capsulitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Enthesitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
High signal intensity (/12)	0	0 – 4	0 – 3	0	0 – 0	0 – 0
Structural lesions						
Erosions (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Fatty lesions (/48)	0	0 – 1	0 – 0	0	0 – 0	0 – 0
Sclerosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Partial ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0

Figure: Baseline MRI T2 short tau inversion recovery (STIR) images of sacroiliac bone marrow edema in a 33-year old postpartum woman.

Conclusion: A very high prevalence of sacroiliac BME on MRI was seen in women immediately postpartum with 64.0% even having a positive MRI for sacroiliitis according to the ASAS definition. A significant decrease in BME was seen over 6 months time, yet a substantial fraction continued to display BME after follow up. History of a recent pregnancy is crucial to take into account when interpreting an MRI-SIJ. In case of a recent pregnancy and clinical suspicion of SpA, it may be wise to postpone MRI-SIJ imaging until at least 6 months after the delivery.

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SLE, Sjögren's and APS – treatment

OP0039

EFFICACY AND SAFETY OF ABATACEPT IN ACTIVE PRIMARY SJÖGREN'S SYNDROME: RESULTS OF A RANDOMISED PLACEBO-CONTROLLED PHASE III TRIAL

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Background: Traditional DMARDs have limited efficacy in primary Sjögren's syndrome (pSS) and, so far, no biologic DMARDs are approved for its systemic treatment. Two open-label studies suggested abatacept (ABA) may have a beneficial effect on disease activity and had an acceptable safety profile in pSS.^{1,2}

Objectives: To examine the efficacy and safety of ABA vs placebo (PBO) in patients (pts) with moderate-to-severe pSS.

Methods: In this Phase III, double-blind, PBO-controlled study (NCT02915159), adult pts meeting the 2016 ACR-EULAR criteria for pSS with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥ 5 were randomised to receive ABA 125 mg SC weekly or PBO for 168 days (24 weeks), followed by a 197-day (365-day in Japan) open-label period of ABA treatment. All pts had a 168-day post-treatment follow-up period. Randomisation was stratified by corticosteroid (CS) and hydroxychloroquine (HCQ) use, enrolment in Japan (yes/no) and stimulated whole salivary flow (SWSF; < 0.1 mL/min). The primary endpoint was mean change in ESSDAI at Day 169. Key secondary endpoints included mean changes in EULAR Sjögren's Syndrome Patient Reported Index and SWSF at Day 169. Other secondary endpoints included objective measures of eye and mouth dryness, DAS28 (CRP), patient-reported outcomes and biomarkers. Hierarchical testing for the primary and two key secondary endpoints was done to preserve overall type I error of 5%.

Results: A total of 187 (ABA, 92; PBO, 95) pts were randomised and received ≥ 1 dose of study drug. Baseline characteristics were comparable between treatment groups: mean (SD) age was 52 (12.9) years, 95% of pts were female, 64% were white, 40% were receiving concomitant stable-dose HCQ and 25% oral CS (≤ 10 mg/day prednisone equivalent). Mean (SD) baseline ESSDAI score was 9.4 (4.3) (ABA, 8.7 [3.4] vs PBO, 10.1 [5.0]). At Day 169, no significant differences were seen between ABA- and PBO-treated pts for the primary or key secondary efficacy outcomes (Table 1). Applying the Benjamini-Hochberg method (with a false discovery rate of 5%) at Day 169, significant treatment differences were observed for 5/12 biomarkers (post hoc analysis) (Table 1). Serious AEs related to the study drug occurred in 3% of ABA- and 1% of PBO-treated pts. Related AEs occurred in

Table 1. Adjusted mean change from baseline (SE) in disease activity and biomarkers at Day 169

	ABA (n=92)	PBO (n=95)	Adjusted mean difference (95% CI)	p value*
Disease activity				
ESSDAI	-3.2 (0.7)	-3.7 (0.7)	0.5 (-0.7, 1.6)	0.4421
ESSPRI	-1.3 (0.3)	-1.5 (0.3)	0.3 (-0.3, 0.8)	0.3367†
SWSF (mL/min)	0.06 (0.09)	0.1 (-0.09)	-0.05 (-0.2, 0.1)	0.5841†
Schirmer's Test, mm/5 minutes	1.7 (1.1)	1.0 (1.1)	0.7 (-1.5, 2.9)	NA
Tear break-up time, seconds	-0.2 (0.4)	-0.3 (0.4)	0.1 (-0.8, 0.9)	NA
Ocular staining score, range 0-12	-1.5 (0.4)	-0.7 (0.4)	-0.7 (-1.6, 0.1)	NA
Biomarkers				
C4 complement, g/L	0.01 (0.0)	-0.01 (0.0)	0.02 (0.01, 0.03)	0.0003
IgA-RF autoantibodies†	-10.4 (2.2)	-1.5 (2.1)	-8.9 (-14.7, -3.1)	0.0028
IgG, g/L	-0.9 (0.3)	0.3 (0.3)	-1.2 (-2.0, -0.4)	0.0041
Kappa light chain, mg/L	-4.7 (1.1)	-0.4 (1.1)	-4.2 (-7.2, -1.2)	0.0052
IgA, mg/L	-57.1 (24.6)	133.6 (52.3)	-190.7 (-336.5, -44.9)	0.0106

*Longitudinal repeated measures model adjusting for the four randomization stratification variables (oral CS use, HCQ use, enrolment in Japan (yes/no), SWSF < 0.1 or ≥ 0.1 mL/min) and baseline value. For biomarker analyses, the Benjamini-Hochberg procedure was applied to control the false discovery rate at an alpha level of 5% (post hoc analysis).

†Normal p values are shown since the primary endpoint was not met.

Units are calculated against standard curves derived from a WHO international reference.

Abb=abatacept; CS=corticosteroid; ESSDAI=EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI=EULAR Sjögren's Syndrome Patient Reported Index; HCQ=hydroxychloroquine; IgA=immunoglobulin A; IgG=immunoglobulin G; IgM=immunoglobulin M; NA=not available; PBO=placebo; p=patient; SWSF=stimulated whole salivary flow.

46% and 25% of ABA- and PBO-treated pts, respectively, but this was not enriched for any specific event and there were no new ABA safety signals.

Conclusion: Despite favourably impacting biomarkers of disease activity, abatacept therapy was no better than PBO for improving the clinical measures of disease. These results do not indicate a clinical benefit of abatacept in pSS.

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OP0040

MODIFIED IMMUNE CELL THERAPY AMELIORATES MURINE LUPUS NEPHRITIS AND INDUCES REGULATORY CELL SUBSETS

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Background: Modified immune cells (MICs) are mononuclear cells that gain immunosuppressive properties after incubation with the proliferation inhibitor mitomycin C. We recently showed that syngeneic MIC therapy controlled experimental autoimmune encephalitis (EAE) (1). In addition, allogeneic MIC therapy prevented rejection in rat heart and hindlimb as well as pig kidney transplantation (2).

Objectives: We now wanted to translate these encouraging findings to the prevention and treatment of lupus nephritis.

Methods: Splenocytes of syngeneic NZB/W F1 (BWF1) donor mice were incubated with mitomycin C and injected into recipient's tail vein after matching for age and disease activity. Group 1 received no MIC therapy, group 2 standard-dose MIC therapy with 1.5×10^8 /kg BW once and group 3 repeated MIC therapy with 1.5×10^8 /kg BW at weeks 1, 2 and 3. Group 4 received MIC infusions before disease onset as preemptive treatment approach. Disease activity was monitored by loss of body weight, protein excretion, serum creatinine and dsDNA antibodies. Combined primary endpoint was day 40 post-treatment, protein excretion ≥ 3 g/l for 2 consecutive weeks and $>30\%$ loss of original body weight. Histopathology with PAS and HE staining was performed to assess degree of lupus nephritis. Regulatory cell subsets were measured in peripheral blood.

Results: MIC therapy prevented the progression of fatal lupus nephritis in BWF1 mice. Protein excretion, serum creatinine and dsDNA antibodies were lower in standard-dose (group 2) and preemptive (group 4) groups compared to control group (group 1) whereas repeated MIC therapy after disease onset had no effect (Figure 1A-E). The primary endpoint was reached significantly more often in control group (group 1, 67%) compared to treatment groups 2 (14%), 3 (14%) and 4 (0%) (Figure 1F). Renal architecture was preserved in different MIC treatment