Objectives: The aims of our study were to assess the 10-year survival of the first TNF- α , to compare retention rates of different anti-TNF drugs in real life settings and to identify factors associated with drug retention in active axSpA.

Methods: We performed a hospital-based retrospective cohort study on consecutive adult axSpA suboptimally controlled by standard therapy, starting their first biological agent with infliximab (IFX), adalimumab (ADA), etanercept (ETA) or golimumab (GLM) according to local policy, recruited at three academic centres between 2003 and July 2018.

Drug efficacy (BASDAI, ASDAS-CRP) as well as reasons for discontinuation were evaluated every 24 weeks. Drug survival was calculated using the Kaplan-Meier analysis, while univariate and multivariate regression was used for predictors of persistence and withdrawal ($p < 0.05$). Subanalysis was done according to discontinuation reasons.

Results: Of the 241 axSpA were recruited, 104 (43.15%) cases received ETA (original, biosimilar), 100 (41.49%) ADA, 26 (10.78%) IFX (original and biosimilar) and 11 cases (4.56%) GLM.

Statistical significant improvement was demonstrated (ASDAS-CRP, BASDAI, BASFI) in all patients, those with higher disease activity and functional impairment at baseline presenting earlier and higher response rate ($p < 0.05$).

We reported high long-term persistence of the first TNF- α with a median survival rate of 8.1 ± 2.1 years for IFX, ADA and ETA; furthermore, at 10 years, up to one third (36%) of axSpA remained on the initial drug achieving either stable remission (62.24%) or low disease activity (37.76%), while one out of five patients on the same drug after 140 months. The retention rates of ETA, ADA and IFX were 70%, 68% and 57% after 3 years; 68%, 48% and 53% after 5 years; 35%, 30% and 27% after 10 years. Overall, retention to ETA was superior to that of monoclonal antibodies ($p < 0.05$), with a total drug-exposure of 625.43 patient-years for ETN, 415.26 for ADA, 221.53 for IFX.

In addition, survival of the second TNF drug was good but inferior to the first TNF- α ($p < 0.05$).

Male sex, age under 40, high baseline C reactive protein, low initial BASFI and disease duration under 5 years were associated with retention rate in multivariate analysis ($p < 0.05$), while the presence of syndesmophytes and obesity with higher withdrawal ($p < 0.05$).

Conclusion: We reported high long-term persistence of the first biological agent in axSpA, with superior retention for ETA compared to monoclonal antibodies. Predictors for high retention rate advocate the rationale for the drug choice in different axSpA settings.

Disclosure of Interests: CODRINA ANCUTA Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly, Cristina Pomirleanu Speakers bureau: Abbvie, Pfizer, UCB, Raluca Paiu: None declared, Georgiana Strugariu Speakers bureau: Abbvie, Pfizer, UCB, Luiza Petrariu Speakers bureau: Abbvie, Pfizer, Novartis, Eugen Ancuta: None declared, Codruta Bran Speakers bureau: Abbvie, Pfizer, Novartis, Lilly, Roche, Rodica Chiriac: None declared, Claudia Mihailov Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly

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FRI0383 PAMIDRONATE IN CHRONIC NON-BACTERIAL OSTEOMYELITIS: A RANDOMIZED, PLACEBO-CONTROLLED PILOT TRIAL

Caroline Marie Andreasen¹, Anne Grethe Jurik², Bent Deleuran^{1,3}, Troels Bille Folkmar⁴, Hans Christian Horn⁵, Troels Herlin⁶, Ellen-Margrethe Hauge^{1,7}.

¹Aarhus University Hospital, Dept. of Rheumatology, Aarhus C, Denmark; ²Aarhus University Hospital, Dept. of Radiology, Aarhus C, Denmark; ³Aarhus University, Department of Biomedicine, Aarhus, Denmark; ⁴Aarhus University Hospital, Dept. of Oral and Maxillofacial Surgery, Aarhus, Denmark; ⁵Odense University Hospital, Dept. of Rheumatology, Odense, Denmark; ⁶Aarhus University Hospital, Paediatrics, Aarhus, Denmark; ⁷Aarhus University, Dept. of Clinical Medicine, Aarhus, Denmark

Background: Chronic non-bacterial osteitis (CNO) is an autoinflammatory disease often associated with seronegative spondyloarthritides. Osteitic bone lesions in adults are predominantly located in the anterior chest wall, the spine and pelvis. Case series suggest that the amino-bisphosphonate pamidronate may be effective in improving bone inflammation, pain, and disability. No randomized controlled trials have been conducted in CNO.

Objectives: In a randomized double-blinded, placebo-controlled trial we hypothesized that pamidronate reduces radiological signs of bone inflammation assessed by whole-body magnetic resonance imaging, improve pain, disability and reduces systemic markers of bone inflammation and bone turnover in blood.

Methods: Patients with an established diagnosis of CNO were assessed for eligibility. Inclusion criteria were 1. Mono- or multifocal bone inflammation (osteitis with or without sclerosis) 2. Jansson clinical score for CNO in children and adults $\geq 39^1$ or malignancy and infection excluded by biopsy and 3. Symptoms duration > 6 weeks. Patients were randomized 1:1 to receive placebo or pamidronate 1 mg/kg, max 60 mg, given for three consecutive days at baseline, week 12 and week 24. Whole-body MRI was performed at baseline, week 12 and 36. CT scan of the anterior chest wall was performed at baseline and week 36. Changes in active and chronic radiological bone inflammation in the ACW and spine were systematically scored.^{2, 3} Patient-reported outcome were measured at baseline and week 1,4,12,24 and 36 using a visual analogue scale for pain and global health assessment, Health Assessment Questionnaire for physical functioning and, EuroQoL-5 Dimension-3 Level and The Short Form (SF)-36 questionnaire for Quality of life. Biomarkers of bone turnover and inflammation in blood were measured at baseline and week 1,4,12,24 and 36.

Results: Analyses were performed in 12 patients with CNO, mean age 32 (range 20-63) years. From baseline to week 36 the radiological score of active bone inflammation decreased from 4.8(SD 2.2) to 2.5(SD 1.6) in the pamidronate group ($p = 0.01$). This differed significantly from the placebo group in which no change from baseline was observed ($p = 0.04$). We observed a decreasing trend in VAS pain from mean 38(SD 23)mm to 19(SD 18)mm and VAS global from 32(SD 22)mm to 13(SD 18)mm.

Conclusion: This study is the first randomized double-blinded, placebo-controlled trial in CNO. Treatment with pamidronate improved bone marrow oedema in the anterior chest wall assessed by whole-body magnetic resonance imaging. This pilot study points out methodological considerations in relation to study design and outcome measures in CNO.

REFERENCES:

- [1] Jansson AF, Müller TH, Gliera L, Ankerst DP, Wintergerst U, Belohradsky BH, et al. Clinical score for nonbacterial osteitis in children and adults. *Arthritis Rheum* 2009;60:1152–9.
- [2] Weber U, et al. Anterior chest wall inflammation by whole-body magnetic resonance imaging in patients with spondyloarthritis: lack of association between clinical and imaging findings in a cross-sectional study. *Arthritis Res Ther* 2012;14:R3.
- [3] Madsen KB, Jurik AG. MRI grading method for active and chronic spinal changes in spondyloarthritis. *Clin Radiol* 2010;65:6–14.

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FRI0384 IMPACT OF INTERLEUKIN 17 BLOCKING AGENT ON CLINICAL OUTCOME IN SAPHO PATIENTS

Gunter Assmann¹, Joerg, Thomas Bittenbring¹, Annette D. Wagner², Martin Schreiber³, Konstantinos Christofyllakis¹, Ulrike Hueffmeier⁴, Claudia Pfoehler⁵, Frank Neumann⁶. ¹University Medical School of Saarland, Medicine I, Oncology and Rheumatology, Homburg, Germany; ²University School of Medicine Hannover, Department of Nephrology, Hannover, Germany; ³Hospital of Worms, Department of Radiology, Worms, Germany; ⁴University Medical School of Erlangen, Human Genetics, Erlangen, Germany; ⁵University Medical School of Saarland, Department of Dermatology, Homburg, Germany; ⁶University Saarland Medical School, Jose Carreras Center for Immunogenetics, Homburg, Germany

Background: SAPHO syndrome has to be considered as a rare subtype of seronegative spondyloarthritis (SpA) showing typical manifestations with palmoplantar pustulosis and osteitis with hyperostosis; the clinical response of conventional or biological disease modifying drugs (DMARDs) in SAPHO syndrome are often disappointing. Whereas in SpA peripheral arthritis and inflammatory back pain represent the leading symptoms, the SAPHO patients often complain painful osteitis with hyperostosis in the sternal region as well as the palmoplantar pustulosis accompanied by synovitis preferentially in large joints including sacroiliitis. Recently, the detection of higher numbers of CD4+IL17+ lymphocytes in the peripheral blood of SAPHO patients has arisen the hypothesis that Th4/17 helper cells with their secretion of interleukin 17 (IL17) could be involved in the development of inflammation in SAPHO syndrome (1)

Objectives: Here we present an observational study of 12 SAPHO patients which were treated with the IL 17 blocking agent secukinumab. In addition, the fraction of CD4/17+ lymphocytes in peripheral blood specimen has been monitored on treatment.

Methods: Between January 2015 and February 2017 clinical activity of disease were measured in 37 SAPHO patients with a disease duration of 11 years (median). The disease activity were evaluated by the osteitis

score and skin score (ranging from 0 to 6, assessed by physician), the HAQ score (ranging from 0 to 3, assessed by patient), and MRI of the osteitis lesion (activity score 0-3, analogously to 3 domains of OMERACT RAMRIS scoring synovitis, bone marrow edema, and erosions; assessed by radiologist). In this period of time 12 of them showed disease activity due to osteitis and/or skin disease, at which time the treatment of secukinumab at dosage of 300mg as monotherapy has been started, re-evaluated after at least 12 weeks (ranging from 12 to 18 weeks). For monitoring blood specimens were derived to assess the CD4+/IL17+ lymphocyte subpopulation using immunofluorescence technique commercial antibodies for CD4, IL17 (Boehringer Ingelheim, Germany). To analyse the differences between the disease activity scores prior to secukinumab treatment and after treatment we applied the nonparametric analysis according to Wilcoxon test. The p-value < 0.05 was considered as significant.

Results: Secukinumab improved osteitis and palmoplantar pustulosis (osteitis score 3.8 to 2.4; p=0.007; PPP 3.4 to 2.4; p=0.071), the HAQ score was reduced from 1.25 to 1.0 (p=0.018), the MRI score from 2.08 to 1.58 (p=0.034). The reduction of at least two clinical activity parameters (osteitis, HAQ and/or MRI) after secukinumab treatment could be documented in all SAPHO patients who showed CD4+/IL17+ lymphocytes in higher frequency of 0.4% of leukocytes of peripheral blood.

Figure: SAPHO patients n1-8 and their CD4/IL17+ lymphocytes fraction in peripheral blood.

Conclusion: Secukinumab seems to control osteitis and PPP in SAPHO syndrome resulting in reduced burden of disease. High Th17 lymphocytes numbers seems to be associated with higher probability of clinical response to secukinumab.

REFERENCE:

- [1] Firinu D, Barca MP, Lorrai MM, Perra S, Cabras S, Muggianu E, Di Martino ML, Manconi PE, Del Giacco SR. TH17 cells are increased in the peripheral blood of patients with SAPHO syndrome. *Autoimmunity*. 2014 Sep;47(6):389-94

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FRI0385

LONG-TERM CERTOLIZUMAB PEGOL TREATMENT OF AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH RAPID AND SUSTAINED REDUCTION OF ACTIVE INFLAMMATION AND MINIMAL STRUCTURAL CHANGES IN THE SPINE: 4-YEAR MRI RESULTS FROM RAPID-AXSPA

Xenofon Baraliakos¹, Sebastian Kruse¹, Simone Auteri², Natasha de Peyrecave², Tommi Nurminen³, Thomas Kümke³, Bengt Hoepken³, Juergen Braun¹.

¹Rheumazentrum Ruhrgebiet and Ruhr-University Bochum, Herne, Germany;

²UCB Pharma, Brussels, Belgium; ³UCB Pharma, Monheim, Germany

Background: In patients (pts) with axial spondyloarthritis (axSpA), inflammation of the spine is believed to trigger a repair mechanism that results in syndesmophyte formation.¹ Fatty lesions (FLs) in the bone marrow and erosions in the axial skeleton, both visible on magnetic resonance imaging (MRI) T1 sequences, are post-inflammatory changes that have been shown to contribute significantly to models predicting new bone formation.² It has previously been shown that resolution of inflammatory lesions (INFLs) in pts with axSpA treated with anti-TNF therapy may be associated with an increase in FLs.^{3,4} RAPID-axSpA was a long-term study in pts with radiographic (r)-axSpA (also known as ankylosing spondylitis) or non-radiographic (nr)-axSpA treated with certolizumab pegol (CZP), which rapidly suppressed active inflammation of the spine, with pts showing limited spinal radiographic progression over 4 years.⁵ However, it is not known whether CZP treatment coincides with changes in FLs, sclerosis, and erosions.

Objectives: To report the incidence and association of active inflammation and chronic lesions in the spine of pts with axSpA treated with CZP over 4 years

Methods: RAPID-axSpA (NCT01087762) was double-blind and placebo (PBO)-controlled to Week (Wk)24, dose-blind to Wk48, and open-label to Wk204. CZP-randomised pts (either 200mg every 2 weeks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO-randomised pts received CZP from Wk24, or if non-responders, from Wk16 onwards. Blinded spinal MRI scans at baseline (BL) and Wk12, 48, 96, and 204 were assessed by 2 central readers to evaluate the presence/absence of active INFLs (Short T1 Inversion Recovery [STIR] sequence) and FLs, sclerosis and erosions (T1 sequence) in vertebral edges (VEs) (present if recorded so by both readers). Pts (r-axSpA and nr-axSpA combined) with valid assessments at BL and at least once post-BL were included. Mean lesion counts at the pt level were estimated from mixed models with repeated measures (MMRM), fitted on observed data from CZP-randomised pts. Associations between INFLs and FLs at the VE level for CZP- and PBO-randomised pts were described using cross-tabulations.

Results: Of 325 randomised pts, 136 were eligible for these analyses. In pts randomised to CZP at Wk0 (n=89), active INFLs were reduced, and FL counts only slightly increased by Wk12; both were sustained at a low level to Wk204 (Table A). Very few VEs with sclerosis and erosions were observed at BL, and no changes in their frequency were observed over 4 years' treatment (Table A). Over 4 years' CZP treatment, the risk of developing a new FL was greater in VEs with vs without INFLs at BL, regardless of changes to INFLs in these VEs post-BL (Table B). The prevalence of FLs was greater in pts with >3 vs ≤3 years' symptom duration and there were more new FLs in the >3 years subgroup during CZP treatment (data not shown)

Conclusion: Long-term CZP treatment in axSpA pts was associated with rapid and sustained reduction in active inflammation and a negligible increase in FLs in VEs. More FLs developed in VEs with INFLs at BL than without, but this was not affected by resolution of INFLs. There was no increase in sclerosis and erosions in VEs over 4 years' CZP treatment.

REFERENCE:

- [1] Appel H. *Curr Rheumatol Rep* 2008;10:356-63; 2. Poddubnyy D. *Arthritis Rheum* 2016;68:1899-903; 3. Maksymowych W. *Ann Rheum Dis* 2013;72:23-8; 4. Song I. *Ann Rheum Dis* 2011;70:1257-63; 5. van der Heijde D. *Ann Rheum Dis* 2018;77:699-705.

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Table: A) Counts of inflammatory lesions, fatty lesions, sclerosis and erosions at the patient level[a] through 204 weeks' CZP treatment (MMRM estimates)

LS mean [SE]	0	12	48	96	204
Inflammatory lesion count	4.9 (0.5)	2.8 (0.4)	2.5 (0.3)	2.7 (0.3)	2.8 (0.4)
Patients observed, n	89	88	68	70	55
Fatty lesion count	6.9 (0.7)	7.3 (0.7)	7.3 (0.8)	7.5 (0.8)	7.4 (0.8)
Patients observed, n	89	88	69	69	55
Sclerosis count	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)
Patients observed, n	89	88	69	69	55
Erosion count	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Patients observed, n	89	88	69	69	55

B) Presence/absence of fatty lesions in vertebral edges[b] through 204 weeks' CZP treatment by baseline MRI lesion type (observed cases)

		Week							
		12		48		96		204	
% of VEs observed [c]		FL+	FL-	FL+	FL-	FL+	FL-	FL+	FL-
FL-INFL+ at baseline n=346	VEs observed, n	338		243		278		205	
	INFL+	8.9	39.3	9.1	26.3	9.4	18.3	11.2	20.5
	INFL-	13.0	38.8	14.0	50.6	22.3	50.0	22.4	45.9
	New FLs, n[d]	74	-	56	-	88	-	69	-
FL-INFL- at baseline n=1866	VEs observed, n	1797		1429		1418		1018	
	INFL+	0.2	4.2	0.5	5.3	0.5	4.2	0.4	5.2
	INFL-	4.7	90.9	6.3	87.9	7.1	88.2	6.9	87.5
	New FLs, n[d]	89	-	97	-	107	-	74	-
FL-INFL+ at baseline n=329	VEs observed, n	326		220		293		220	
	INFL+	42.9	4.9	34.5	4.5	31.1	1.4	30.9	1.8
	INFL-	46.9	5.2	57.3	3.6	61.4	6.1	60.5	6.8
	VEs observed, n	575		424		494		337	
FL-INFL- at baseline n=586	VEs observed, n	575		424		494		337	
	INFL+	10.6	0.9	6.1	1.2	7.3	1.4	7.4	1.2
	INFL-	76.7	11.8	78.8	13.9	78.1	13.2	75.1	16.3

MRI Set, [a] Week 0 CZP patients only (n=89), [b] All CZP-treated patients, including those switching from PBO to CZP treatment at Weeks 16/24, [c] Unless stated otherwise, [d] The number of observed VEs FL+ at BL recorded as FL+ post-BL. CZP: certolizumab pegol; FL: fatty lesion; INFL: inflammatory lesion; LS: least squares; MMRM: mixed model repeated measures; MRI: magnetic resonance imaging; PBO: placebo; SE: standard error; VE: vertebral edge.