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 pustolosis (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.

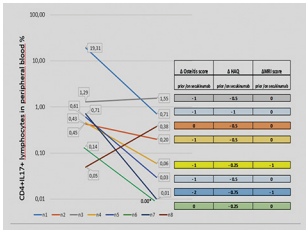

Figure: SAPHO patients n1-8 and their CD4/17+ lymphocytes fraction in peripheral blood.

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.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4145

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 Baraliakos[1], Sebastian Kruse[1], Simone Auteri[2], Natasha de Peyrecave[2], Tommi Nurminen[3], Thomas Kumke[3], Bengt Hoepken[3], Juergen Braun[1].
[1]Rheumazentrum Ruhrgebiet and Ruhr-University Bochum, Herne, Germany; *[2]UCB Pharma, Brussels, Belgium*; *[3]UCB 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.

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Acknowledgement: We thank the patients who participated. This study was funded by UCB Pharma, medical writing by Hinal Tanna, Costello Medical, UK.

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)	Week 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)

% of VEs observed [c]		Week 12 FL+	12 FL−	48 FL+	48 FL−	96 FL+	96 FL−	204 FL+	204 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**
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.

Disclosure of Interests: Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Sebastian Kruse: None declared, Simone Auteri Employee of: Employee of UCB Pharma, Natasha de Peyrecave Employee of: Employee of UCB Pharma, Tommi Nurminen Employee of: Employee of UCB Pharma, Thomas Kumke Employee of: UCB Pharma, Bengt Hoepken Employee of: Employee of UCB Pharma, Juergen Braun Shareholder of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbott, Bristol Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Consultant for: Abbott, Bristol Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB-

DOI: 10.1136/annrheumdis-2019-eular.689

FRI0386

RELATIONSHIP BETWEEN ASDAS STATES AND INHIBITION OF STRUCTURAL DAMAGE PROGRESSION WITH SECUKINUMAB IN ANKYLOSING SPONDYLITIS: DATA FROM MEASURE 1 TRIAL

Xenofon Baraliakos[1], Helena Marzo-Ortega[2], Filip van den Bosch[3], Atul Deodhar[4], Erhard Quebe-Fehling[5], Eumorphia Maria Delicha[5], Zsolts Talloczy[6], Corine Gaillez[5]. *[1]1Rheumazentrum Ruhrgebiet, Ruhr University Bochum, Herne, Germany*; *[2]NIHR LBRC, Leeds Teaching Hospitals Trust and LIRMM, Unversity of Leeds, Leeds, United Kingdom*; *[3]Ghent University Hospital, Ghent, Belgium*; *[4]Oregon Health and Science University, Oregon, United States of America*; *[5]Novartis Pharma AG, Basel, Switzerland*; *[6]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*

Background: The primary treatment goal in patient with axial Spondyloarthritis (axSpA) is to optimize health-related quality of life through control of signs and symptoms, no structural damage progression and preservation of function.[1] The 2017 Treat to Target recommendations (T2T) outlined Ankylosing Spondylitis Disease Activity Score (ASDAS) -inactive disease (ID) as an optimal treatment target for axSpA patients.[1] ASDAS states were shown to correlate with syndesmophyte formation as assessed with X-Ray and MRI changes.[2] Secukinumab, a fully human monoclonal antibody that directly inhibits IL-17A, demonstrated sustained efficacy and low radiographic progression through 4 years in patient with ankylosing spondylitis (AS) in MEASURE 1 study (NCT01863732).[3]
Objectives: To investigate the relationship between ASDAS states and inhibition of radiographic structural progression in patient with AS treated with secukinumab 150 mg from the MEASURE 1 study over 4-years using *post hoc* analysis.
Methods: Lateral radiographs of the cervical and lumbar spine were assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS: range 0-72). Images were scored twice at baseline/Week (Wk) 104 and baseline/Wk 208 by 2 central readers blinded to treatment/visit; mean change from baseline to Wk 104 or 208 in mSASSS scores were used. The ASDAS-CRP was used to define the disease activity states at Wks 16, 52, 104, and 208: ID (ASDAS-CRP < 1.3), Low Disease Activity (LDA, 1.3 ≤ ASDAS-CRP < 2.1) or pooled High/Very High Disease Activity (HDA/VHDA, ASDAS-CRP ≥ 2.1) given low number of patients with VHDA. Sustained ASDAS state at Wk 104 was defined as reaching the same state at Wk 104 and Wk 16 and/or 52. Sustained ASDAS state at Wk 208 was defined as reaching the same state at Wk 208 and Wk 16 and/or 52. Overall, 87 patients on secukinumab 150 mg were in the extension trial; of these, 57 and 71, respectively, had evaluable X-rays at Wks 104 and 208.
Results: The proportion of patients achieving each ASDAS state are shown in **Table**. Patients with ASDAS-ID were associated with numerically lower mSASSS mean change from baseline to Wks 104/208 compared to other ASDAS states (**Figure**).
Conclusion: In this *post hoc* analysis, patients with ASDAS-ID state and sustained ASDAS-ID state had lower radiographic progression than patients with higher disease activity at 2 and 4-years suggesting a potential relationship between ASDAS state and structural progression in patients with AS. Further confirmation is needed in larger prospective studies.

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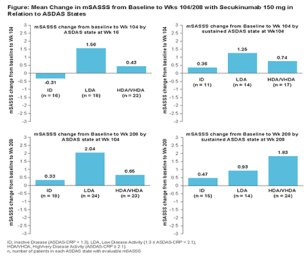
Table: Proportion of Patients with ASDAS States through Wk 208

ASDAS states	Wk 16 N = 86	Wk 52 N = 84	Wk 104 N = 80	Wk 208 N = 78
ID	24.4	25.0	30.0	26.9
LDA	34.9	39.3	38.8	33.3
HDA/VHDA	40.7	35.7	31.3	39.7

ID, Inactive Disease (ASDAS-CRP < 1.3); LDA, Low Disease Activity (1.3 ≤ ASDAS-CRP < 2.1); HDA/VHDA, High/very high Disease Activity (ASDAS-CRP ≥ 2.1)
N, total number patients with ASDAS



Disclosure of Interests: Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Helena Marzo-Ortega Grant/research support from: Janssen, Novartis and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Speakers bureau: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB., Atul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Erhard Quebe-Fehling Shareholder of: Novartis, Employee of: Novartis, Eumorphia Maria Delicha Employee of: Novartis, Zsolts Talloczy Shareholder of: Novartis, Employee of: Novartis, Corine Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis

DOI: 10.1136/annrheumdis-2019-eular.1255