REFERENCES:

- [1] van der Horst-Bruinsma IE, et al. *Ann Rheum Dis*. 2019;78:1550-1558.
- [2] Zhao SS, et al. *Rheumatology*. 2019;58:2025-2030.
- [3] Deodhar A, et al. *Lancet*. 2020;395:53-64.

Table 1. Baseline Characteristics of Patients Categorised by Sex

Characteristic	Patients with r-axSpA (COAST-V/W)			Patients with nr-axSpA (COAST-X)		
	(n=376)			(n=198)		
	Male (n=298)	Female (n=78)	p value	Male (n=99)	Female (n=99)	p value
Age at onset (yrs), mean (SD)	26.5 (8.7)	30.1 (10.1)	0.002*	27.9 (7.7)	32.0 (10.7)	0.002*
Symptom duration (yrs), mean (SD)	16.7 (10.5)	17.8 (12.2)	0.420	9.5 (9.2)	12.3 (11.3)	0.057
ASDAS, mean (SD)	4.0 (0.8)	3.9 (0.7)	0.304	3.7 (0.8)	3.9 (0.8)	0.143
BASDAI, mean (SD)	7.10 (1.4)	7.4 (1.5)	0.179	6.9 (1.4)	7.4 (1.4)	0.013*
Fatigue/tiredness (BASDAI Q1), mean (SD)	7.4 (1.6)	7.8 (1.5)	0.036*	7.0 (1.6)	7.9 (1.5)	<0.001*
Spinal pain (BASDAI Q2), mean (SD)	7.9 (1.5)	8.0 (1.5)	0.682	7.5 (1.4)	7.9 (1.5)	0.029*
Pain/swelling in other joints (BASDAI Q3), mean (SD)	6.5 (2.1)	6.9 (2.2)	0.129	6.6 (2.3)	7.2 (1.9)	0.039*
Tenderness to touch/pressure (BASDAI Q4), mean (SD)	6.8 (1.8)	7.0 (1.9)	0.339	6.6 (1.9)	6.8 (1.8)	0.404
Morning stiffness (BASDAI Q5), mean (SD)	7.5 (1.6)	7.7 (1.8)	0.504	7.3 (1.7)	7.7 (1.9)	0.137
Morning stiffness duration (BASDAI Q6), mean (SD)	6.5 (2.3)	6.5 (2.8)	0.944	6.3 (2.3)	6.6 (2.5)	0.392
Spinal pain at night NRS, mean (SD)	7.4 (1.5)	7.8 (1.7)	0.033*	7.0 (1.8)	7.6 (1.8)	0.027*
BASFI, mean (SD)	6.8 (1.8)	7.0 (2.0)	0.466	6.2 (1.8)	6.7 (2.1)	0.108
SF-36 PCS, mean (SD)	30.9 (8.3)	28.9 (8.2)	0.075	33.1 (7.7)	32.1 (7.2)	0.348

p-value from Fisher's exact test analysis of variance (ANOVA) with sex as a factor for continuous data. Data includes pooled IXEQ2W and IXEQ4W.

COAST-VW Male & Female
ASAS40 (ITT, NRI)

Figure 1. COAST-VW ASAS40 (ITT, NRI) Patients initially randomized to PBO in COAST-VW switched to IXEQ2W or Q4W at week 16 by study design; PBO data are summarised up to week 16.

Acknowledgements: Writing support was provided by Dr Geraldine Fahy, an employee of Eli Lilly and Company

Disclosure of Interests: Irene van der Horst-Bruinsma Speakers bureau: BMS, AbbVie, Pfizer, UCB, MSD, Consultant of: AbbVie, UCB, MSD, Lilly, Novartis, Grant/research support from: MSD, Pfizer, AbbVie, Rebecca Bolce Shareholder of: Eli Lilly, Employee of: Eli Lilly, Theresa Hunter Shareholder of: Eli Lilly, Employee of: Eli Lilly, David Sandoval Shareholder of: Eli Lilly, Employee of: Eli Lilly, Danting Zhu Employee of: Eli Lilly, Vladimir J. Geneus Employee of: Eli Lilly, Jeffrey Lisse Shareholder of: Eli Lilly, Employee of: Eli Lilly, Soyi Liu League Shareholder of: Eli Lilly, Employee of: Eli Lilly, Marina Magrey Consultant of: Novartis, Eli Lilly, Pfizer, AbbVie, UCB and Jansen, Grant/research support from: Amgen, AbbVie, and UCB Pharma
DOI: 10.1136/annrheumdis-2021-eular.684

POS0229

DISEASE ACTIVITY AND INFLAMMATION FOLLOWING WITHDRAWAL OF CERTOLIZUMAB PEGOL TREATMENT IN AXIAL SPONDYLOARTHRITIS PATIENTS WHO DID NOT EXPERIENCE FLARES DURING THE C-OPTIMISE STUDY

L. S. Gensler¹, X. Baraliakos², L. Bauer³, B. Hoepken³, T. Kümke³, M. Kim⁴, R. B. M. Landewé^{5,6}. ¹University of California San Francisco, Department of Rheumatology, San Francisco, United States of America; ²Ruhr-University Bochum, Rheumazentrum Ruhrgebiet Herne, Herne, Germany; ³UCB Pharma, N/A, Monheim am Rhein, Germany; ⁴UCB Pharma, N/A, Smyrna, United States of America; ⁵Amsterdam University Medical Center, Department of Rheumatology & Clinical Immunology, Amsterdam, Netherlands; ⁶Zuyderland Medical Center, Department of Rheumatology, Heerlen, Netherlands

Background: C-OPTIMISE was a phase 3b clinical trial investigating certolizumab pegol (CZP) maintenance dose continuation, reduction or withdrawal following achievement of sustained remission in patients with axial spondyloarthritis (axSpA). During the C-OPTIMISE maintenance period, the majority of patients randomised to CZP, either the full or reduced maintenance dose, did not experience disease flares. Conversely, in those who had CZP withdrawn, only a minority of patients remained flare-free.¹

Objectives: This post-hoc analysis evaluates disease activity and clinical markers of inflammation in patients who did not experience a disease flare following randomisation to CZP full maintenance dose, CZP reduced maintenance dose or placebo (PBO) during the maintenance period (Weeks 48–96) of C-OPTIMISE.

Methods: C-OPTIMISE (NCT02505542) was a multicentre, double-blind, parallel-group, randomised phase 3b study with a 48-week open-label run-in period.¹ Adult patients with early (<5 years' symptom duration) active axSpA received open-label CZP 200 mg every 2 weeks (Q2W) for the first 48 weeks; from Week 48, patients who achieved sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS] <1.3 at Week 32 or 36 and Week 48) were randomised 1:1:1 to double-blind CZP 200 mg Q2W (full maintenance dose), CZP 200 mg Q4W (reduced maintenance dose) or PBO for a further 48 weeks (maintenance period). A flare was defined as ASDAS ≥2.1 at two consecutive visits or ASDAS >3.5 at any visit. We report ASDAS, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and C-reactive protein (CRP) and fecal calprotectin levels during Weeks 48–96 in CZP- and PBO-randomised patients who did not experience a flare (i.e. completed Week 96 on randomised treatment). Missing data were imputed using last observation carried forward.

Results: Of 313 patients entering the maintenance period at Week 48, 197 (62.9%) completed Week 96 on randomised treatment without experiencing a flare; of these, 89 (85.6%) and 84 (80.0%) patients were in the CZP 200 mg Q2W and CZP 200 mg Q4W arm, respectively, with only 24 (23.1%) patients randomised to PBO not experiencing a flare. Baseline characteristics of these patients are shown in the Table 1. During Weeks 48–96, disease activity (ASDAS, BASDAI) and CRP levels were comparable between the CZP full and reduced maintenance dose group, and lower in both CZP arms than in PBO (Figure 1 A–C). From Week 60 up to Week 96, PBO patients who did not flare had consistently higher mean ASDAS, BASDAI and CRP levels compared with CZP-randomised patients (Figure 1 A–C). Similarly, there was a greater increase in fecal calprotectin levels between Weeks 48 and 96 in the PBO arm compared with both CZP arms (Figure 1 D).

Conclusion: Despite not meeting the threshold for a flare, consistently higher disease activity and increases in serologic and inflammatory biomarkers were observed in PBO-randomised patients who did not experience a flare during the C-OPTIMISE study compared to those who remained on CZP. These findings confirm that patients with axSpA who achieve sustained remission benefit from continued CZP treatment, either with the full or reduced maintenance dose, over treatment withdrawal.

REFERENCES:

- [1] Landewé R. *Ann Rheum Dis* 2020;79:920–8.

Table 1. Baseline (Week 0) characteristics of patients who did not experience flares during the C-OPTIMISE maintenance period

	Placebo (n=24)	CZP 200 mg Q4W (n=84)	CZP 200 mg Q2W (n=89)
Age (years), mean (SD)	29.8 (7.4)	32.9 (6.7)	32.4 (7.2)
Male, n (%)	19 (79.2)	69 (82.1)	69 (77.5)
Time since diagnosis (years)			
Mean (SD)	2.0 (1.8)	2.0 (1.7)	2.5 (1.6)
Median	1.2	1.2	2.7
Symptom duration (years)			
Mean (SD)	2.7 (1.7)	3.4 (1.9)	3.9 (2.9)
Median	2.8	3.5	3.9
ASDAS, mean (SD)	3.4 (0.8)	3.7 (0.8)	3.7 (0.7)
BASDAI, mean (SD)	6.3 (1.1)	6.6 (1.5)	6.4 (1.4)
CRP (mg/L), geometric mean	6.28	7.88	7.35
Fecal calprotectin (µg/g), mean (SD)	71.8 (111.4)	87.1 (110.5)	81.0 (120.0)

SD: standard deviation.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

Figure. (A) ASDAS, (B) BASDAI, (C) CRP and (D) fecal calprotectin in patients who did not experience a flare during the C-OPTIMISE maintenance period (Weeks 48–96)

Missing data were imputed using last observation carried forward. Δ values for fecal calprotectin show change from Week 48. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; CZP: certolizumab pegol; Q2W/Q4W: every 2/4 weeks.

Disclosure of Interests: Lianne S. Gensler Consultant of: AbbVie, Eli Lilly, Gilead, GSK, Novartis, Pfizer, UCB Pharma, Grant/research support from: Pfizer, Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Merck, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Merck, Novartis, Lars Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, Bengt Hoepken Shareholder of: UCB Pharma, Employee of: UCB Pharma, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Mindy Kim Shareholder of: UCB Pharma, Employee of: UCB Pharma, Robert B.M. Landewé Speakers bureau: Abbott, Amgen, BMS, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Consultant of: Abbott, Ablynx, Amgen, AstraZeneca, BMS, Centocor, GSK, Merck, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth

DOI: 10.1136/annrheumdis-2021-eular.1547

POS0230

INTESTINAL MICROBIOTA CHANGES TNF-INHIBITORS INDUCED IN IBD-RELATED SPONDYLOARTHRITIS

M. C. Ditto¹, S. Parisi¹, G. Landolfi², R. Borrelli¹, G. Caviglia³, D. G. Ribaldone⁴, M. Astegiano⁴, A. Zanetti², G. Carrara², C. A. Scirè², M. Antivalle⁵, P. Sarzi-Putini⁵, E. Fusaro¹. ¹AOU Città della Salute e della Scienza di Torino, Rheumatology Unit, Turin, Italy; ²Italian Society for Rheumatology, Epidemiology Research Unit, Milan, Italy; ³University of Turin, Medical Sciences, Turin, Italy; ⁴AOU Città della Salute e della Scienza di Torino, Gastroenterology Unit, Turin, Italy; ⁵ASST Fatebenefratelli-Sacco, Rheumatology Unit, Milan, Italy

Background: the close relationship between joints and gut inflammation has long been known and several data suggest that the dysbiosis could represents the link between Spondyloarthritis (SpA) and Inflammatory Bowel Diseases (IBD). To date, the manipulation of the intestinal microbiota is considered the key to the cure or control of the natural history of several pathologies sustained or favored by dysbiosis. The introduction of biologic drugs, in particular Tumor Necrosis Factor inhibitors (TNFi), revolutionized the management of both these diseases, thanks to the strong inhibition of inflammation and partially indirectly with mechanisms not yet fully clarified. While the impact of conventional drugs on gut microbiota is well known poor data are available about TNFi.

Objectives: to investigate the impact of TNFi on gut microbiota.

Methods: we included CD or UC patients fulfilling criteria for axial or peripheral SpA (ASAS 2009) on a typical Mediterranean diet, naïve to biologics needing TNFi. Clinical history, physical examination, instrumental examinations, biochemical

examination including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), HLA-B27 and fecal calprotectin at the baseline and after 6 months were performed. TNFi included infliximab and adalimumab. Fecal samples were collected by patients themselves by 24 hours before the start of the therapy. The processing was performed through metagenomic NGS (next generation sequencing) including the amplification of the V3 and V4 regions of the 16S (V3 and V4) and sequencing on the Illumina MiSeq platform. All patients received the treatment at least until week 24. Clinical disease indices included Visual Analogue Scale (VAS)-pain and Visual Analogue Scale (VAS)-disease activity for all patients, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for axial involvement, clinical disease activity index (CDAI) and Health Assessment Questionnaire-Disability Index (HAQ-DI) for peripheral involvement, Harvey-Bradshaw Index for CD (HBI), or partial Mayo (pMayo) score for UC, were assessed at baseline and at the end of the study. The study was approved by the ethics committee (approval code 0056924).

Results: we evaluated 20 patients affected by enteropathic arthritis, naïve for biologic drugs, treated with TNFi. After six months of therapy we observed a significant increase in Lachnospiraceae family ($\Delta +10.3$, $p 0.04$) and in Coprococcus genus ($\Delta +2.8$, $p 0.003$). We also observed a decrease trend in Proteobacteria ($\Delta -8.0$ $p 0.095$) and Gammaproteobacteria ($\Delta -9$, $p 0.093$) and an increase trend in Clostridia ($\Delta +8.2$ $p 0.083$). We didn't find differences between TNFi responders (SpA improvement or IBD remission achieved) and not responders in terms of alpha and beta-diversity.

Conclusion: the decrease of Proteobacteria and the increase of Lachnospiraceae and Coprococcus is consistent with the hypothesis that TNFi therapy, by decreasing inflammation, tends to restore the intestinal eubiosis. However further studies on larger cohort including the evaluation of gut virota and microbiota will be necessary to definitively clarify the effects of TNFi on the composition and function of the gut microbiota.

REFERENCES:

- [1] Bazin T et al. *Sci Rep*. 2018;8(1):5446.
- [2] Aden K et al. *Gastroenterology*. 2019;157(5):1279-1292.e11.

Table 1. Comparison between clinical variables between baseline and T6 (six months)

Clinical variables	T0	T6	P_value
Fecal Calprotectin(µg/g)- median (IQR)	207.5(125.5-446.2)	81(50-197.2)	0.004
CRP(mg/L)- median(IQR)	8.2(4.8-20.8)	2.9(1-4)	0.001
ESR(mm/h)- median(IQR)	21.5(10.8-34)	11(7.8-21)	0.003
VAS_pain- median(IQR)	50(38.8-60)	35(10-42.5)	0.001
VAS_disease- median(IQR)	50(38.8-60)	37.5(25-42.5)	0.006
HAQ- mediana(IQR)	0.6(0.1-0.8)	0.2(0.1-0.6)	0.004
BASDAI_score- median(IQR)	5.2(4.1-5.6)	2.8(2.5-4.3)	0.013
CDAI_activity- median(IQR)	13(10.5-16)	7(5.2-11)	0.004
IBD activity n(%) - 0	11 (55%)	20 (100%)	0.174
IBD activity n(%) - 1	6 (30%)	0 (0%)	
IBD activity n(%) - 2	2 (10%)	0 (0%)	
IBD activity n(%) - 3	1 (5%)	0 (0%)	

Disclosure of Interests: None declared.

Figure 1. Comparison between Lachnospiraceae and Coprococcus at the baseline (T0) and after 6 months (T6) of therapy.

DOI: 10.1136/annrheumdis-2021-eular.1589

POS0231

IMPACT OF GENDER AND COMORBIDITIES IN ENTEROPATHIC SPONDYLOARTHRITIS: A CROSS-SECTIONAL STUDY

A. D'Antonio¹, M. S. Chimenti¹, P. Conigliaro¹, P. Triggianese¹, S. Ferrigno¹, M. Ferraioli¹, B. Neri², L. Biancone², R. Perricone¹. ¹University of Rome Tor Vergata, Rheumatology, Allergy and Clinical Immunology, Rome, Italy; ²University of Rome Tor Vergata, GI Unit, Rome, Italy

Background: Enteropathic Spondyloarthritis (ESpA) belongs to the group of Spondyloarthritis (SpA) typically associated with inflammatory bowel disease (IBD). SpA are divided into axial (ax) or peripheral disease. Ax-SpA are classified as