Biocad, Gilead, GlaxoSmithKline, Eli Lilly, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis, and Pfizer

DOI: 10.1136/annrheumdis-2021-eular.761

POS0909

IXEKIZUMAB IMPROVES SIGNS, SYMPTOMS AND QUALITY OF LIFE OF ANKYLOSING SPONDYLITIS IN PATIENTS IRRESPECTIVE OF HLA-B27 STATUS: POOLED RESULTS FROM THE COAST-V AND COAST-W TRIALS

J. D. Reveille¹, P. Rahman², D. Sandoval³, T. Muram⁴, R. Bolce⁴, S. Y. Park⁴, M. Rudwaleit⁵. ¹University of Texas Houston, Department of Internal Medicine, Houston, United States of America; ²Memorial University of Newfoundland, Clinical Research, St. John's, Canada; ³Eli Lilly and Company, Immunology, Indianapolis, United States of America; ⁴Eli Lilly and Company Corporate Center, Immunology, Indianapolis, United States of America; ⁵Charité - Campus Benjamin Franklin (Berlin), Rheumatology, Berlin, Germany

Background: Human leukocyte antigen-B27 (HLA-B27) is found in most patients (pts) with ankylosing spondylitis (AS). Although a subset of pts with AS are HLA-B27 negative (NEG), ensuring treatment efficacy in this subpopulation is important.

Objectives: This analysis evaluated the efficacy of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, in AS pts who are either HLA-B27 positive (POS) or NEG.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were 2 phase 3, multicenter, randomized, double-blind, PBO-controlled trials investigating the efficacy of 80-mg IXE administered every 4 weeks (Q4W) and every 2 weeks (Q2W) in pts naïve to biological disease-modifying anti-rheumatic drugs (bDMARDs; COAST-V) and in those who were inadequate responders or intolerant to 1 or 2 tumor necrosis factor inhibitors (TNFi; COAST-W). Only data from pts randomized at baseline to PBO, IXE Q4W or Q2W in both trials who met per protocol eligibility criteria were integrated and stratified based on HLA-B27 status (POS, NEG) for an *ad hoc* subgroup analysis. Efficacy was assessed using the Assessment of Spondyloarthritis International Society 40 (ASAS40), Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) and Short Form 36 Physical Component Scores (SF-36 PCS). Missing data were imputed by non-responder imputation (NRI) for binary measure and by modified baseline observation carried forward (mBOCF). Data from PBO was reported up to Week 16 and for pooled IXE Q4W and Q2W up to Week 52.

Results: This analysis includes pts with AS who are HLA-B27 POS (N=453; PBO=155, IXE=298) or NEG (N=62, PBO=21, IXE=41). Overall, more pts were male (82.6%, POS; 77.4%, NEG), and for IXE treated pts, the duration of disease since r-axSpA diagnosis was 10.3 (SD=9.1) and 6.9 (SD=5.6) years, among POS and NEG pts respectively (Table 1). Among IXE treated patients,

Table 1. Baseline Characteristics by HLA-B27 Positive and Negative Status

	Positive HLA-B27		Negative HLA-B27	
	PBO (N=155)	IXE (N=298)	PBO (N=21)	IXE (N=41)
Male, n (%)	133 (85.8)	241 (80.9)	18 (85.7)	30 (73.2)
Age of r-axSpA onset (yr), mean (SD)	25.2 (9.28)	26.3 (8.38)	35.4 (8.43) [‡]	34.6 (10.32) [‡]
Duration of symptoms since r-axSpA onset (yr)	18.7 (11.82)	17.1 (10.38)	16.0 (9.69)	15.9 (12.40)
C-Reactive protein (mg/L), mean (SD)	16.7 (22.43)	16.9 (25.50)	18.1 (21.69)	13.7 (14.38)
ASDAS score, mean (SD)	4.0 (0.78)	4.0 (0.83)	4.3 (0.76)	4.1 (0.73)
BASDAI score, mean (SD)	7.1 (1.25)	7.2 (1.37)	7.6 (1.31) [*]	7.4 (1.41)
SF-36 PCS, mean (SD)	33.7 (7.50)	33.2 (7.63)	34.1 (8.28)	31.4 (7.67)

Abbreviations: ASDAS, Assessment of Spondyloarthritis International Society 40; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; N, total number of patients in group; n, number of patients in category/subgroup; PBO, placebo; r-axSpA, axial spondyloarthritis; SD, standard deviation; SF-36 PCS, Short Form 36 Physical Component Scores; yr, years. *p*-value: vs. HLA-B27 positive: ^{*}≤0.05, [‡]<0.0001

the mean age of HLA-B27 NEG pts was approximately 7-8 years older than HLA-B27 POS pts. At Week 16, 39.6% (n=118/298) of HLA-B27 POS and 29.3% (n=12/41) of HLA-B27 NEG pts achieved ASAS40, and 34.6% (n=103) of HLA-B27 POS and 17.1% (n=7) of HLA-B27 NEG pts achieved BASDAI50; improvements were seen as early as Week 1 and sustained or improved up to Week 52. The mean baseline SF-36 PCS was 33.2 (SD=7.63) for HLA-B27 POS and 31.4 (SD=7.67) for HLA-B27 NEG pts. At Week 16, the mean change from baseline in SF-36 PCS was 7.3 (SD 7.6) for HLA-B27 POS and 3.7 (SD=6.83) for HLA-B27 NEG pts. Improvements were sustained to Week 52 (Figure 1).

Conclusion: IXE improves signs, symptoms, patient-reported outcomes and health-related quality of life in HLA-B27 POS and NEG pts with AS, however the HLA-B27 POS pts have a faster and more robust response than HLA-B27 NEG pts.

Figure 1. Proportion of patients achieving ASAS40 by HLA-B27 Positive and Negative Status in patients randomized to placebo up to Week 16 and ixekizumab up to Week 52

Abbreviations: ASAS40, Assessment of Spondyloarthritis International Society 40; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; NRI, nonresponder imputation

Figure 1. Comparisons done using t-test and chi-square test for continuous and categorical variables.

Disclosure of Interests: John D Reveille Consultant of: UCB (Union Chimique Belge), Eli Lilly, Novartis, and Pfizer, Grant/research support from: Janssen 2018; Eli Lilly 2020, Proton Rahman Speakers bureau: Abbott, AbbVie, Amgen, Bristol-Meyers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Consultant of: Abbot, AbbVie, Amgen, Bristol-Meyers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Grant/research support from: Janssen and Novartis, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Talia Muram Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, So Young Park Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Martin Rudwaleit Speakers bureau: AbbVie, Bristol-Meyers Squibb, Chugai, Janssen, Eli Lilly, MSD (Merck Sharp and Dohme), Novartis, Pfizer, UCD (Union Chimique Belge), Consultant of: AbbVie, Janssen, Eli Lilly, Novartis, Pfizer, UCB (Union Chimique Belge)

DOI: 10.1136/annrheumdis-2021-eular.801

POS0910

EVALUATION OF THE NONSTEROIDAL ANTI-INFLAMMATORY DRUG-SPARING EFFECT OF SECUKINUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS OF THE MULTICENTER, RANDOMISED, DOUBLE-BLIND, PHASE IV ASTRUM-TRIAL

U. Kiltz^{1,2}, X. Baraliakos^{1,2}, J. Brandt-Juergens³, U. Wagner⁴, S. Lieb⁵, C. Sieder⁵, C. Mann⁵, J. Braun^{1,2} on behalf of The study was sponsored by Novartis Pharma GmbH, Germany. ¹Rheumazentrum Ruhrgebiet, Claudiusstraße, Herne, Germany; ²Ruhr-Universität Bochum, Universitätsstraße, Bochum, Germany; ³Rheumatologische Schwerpunktpraxis, Seelbergstraße, Berlin, Germany; ⁴Universitätsklinikum Leipzig AöR, Medizinische Klinik und Poliklinik 3 für Endokrinologie,

Nephrologie, Rheumatologie, Sektion Rheumatologie, Leipzig, Germany;

⁵Novartis Pharma GmbH, Immunology, Hepatology and Dermatology, Nürnberg, Germany

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory back pain in patients (pts) with ankylosing spondylitis (AS). However, an increased risk of side effects associated with NSAIDs and their dosage has been reported¹. Therefore, lower doses and a dose reduction is desirable.

Objectives: To evaluate the short-term NSAID sparing effect of secukinumab (SEC) in AS pts with NSAID intake.

Methods: In a prospective controlled trial, 211 adult pts with active AS (BASDAI ≥ 4) and an inadequate response (IR) to at least 2 NSAIDs at the highest recommended/tolerated dose and pts with an IR, or those who were naïve/intolerant to a maximum of 2 tumour necrosis factor inhibitors (TNFi) were enrolled. NSAID intake was evaluated using the ASAS-NSAID score. To be eligible, pts had to take at least 50% of the highest recommended/tolerated NSAID dose regularly. Pts were randomised (1:1:1) to receive SEC 150 mg s.c. from Week (Wk) 0 (group [gp] 1), Wk 4 (gp 2) and Wk 16 (gp 3). All groups received SEC 150 mg from Wk 16. NSAID tapering was allowed in all groups from Wk 4 onwards. The primary endpoint (PE) was an ASAS20 response of pooled gp 1 and gp 2 vs. gp 3 at Wk 12.

Results: There were 71 pts in gp 1, 70 in gp 2 and 70 in gp 3. Baseline (BL) characteristics were comparable across groups; mean age (SD) was 45.2

Table 1. Effect of SEC 150 mg s.c. in AS pts (Intention-to-Treat population) at Wk 16

(%), unless otherwise specified	Group 1 (N=71) (SEC 150 mg from BL until Wk 20)	Group 2 (N=70) (PBO from BL until Wk 4; SEC 150 mg from Wk 4)	Group 3 (N=70) (PBO from BL until Wk 16; SEC 150 mg from Wk 16)
ASAS20*	56.3	50.0	41.4
ASAS40*	43.7 [§]	32.9	21.4
ASAS5/6*	39.4 [‡]	32.9	21.4
ASAS-PR*	8.5	20.0 [‡]	5.7
ASAS20			
TNF-IR**	60.0 ^{††}	26.3	45.0
TNF-naïve**	54.9	58.8 [‡]	40.0
ASAS40			
TNF-IR**	45.0	15.8	25.0
TNF-naïve**	43.1 [‡]	39.2 [‡]	20.0
ASDAS-CRP change (mean $\pm$ SD)**	-1.2 $\pm$ 0.9 [§]	-1.0 $\pm$ 0.9 [‡]	-0.7 $\pm$ 0.8
BASDAI change (mean $\pm$ SD)***	-2.3 $\pm$ 1.9 [‡]	-2.0 $\pm$ 2.0	-1.7 $\pm$ 2.0
BASDAI50*	32.4	28.6	22.9
ASAS-NSAID score change (mean $\pm$ SD)**	-51.5 $\pm$ 46.2 [‡]	-42.5 $\pm$ 68.6	-33.7 $\pm$ 38.8
ASAS-NSAID score decrease $\geq$ 50%*	64.8 [‡]	58.6	42.9
$<10^*$	52.1 [§]	45.7 [‡]	28.6
$=0^*$	32.4 [‡]	38.6 [§]	17.1

AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis International Society; ASDAS, AS Disease Activity score; BASDAI, Bath AS Disease Activity Index; BL, baseline; CRP, C-reactive protein; IR, inadequate responder; NSAID, nonsteroidal anti-inflammatory drug; N, total number of subjects in each treatment gp; PBO, placebo; PR, partial remission; pts, patients; SEC, secukinumab; TNFi, tumour necrosis factor inhibitor; Wk, week. [†]p<0.001; [§]p<0.01 and [‡]p<0.05 vs. gp 3; ^{††}p<0.05 vs. gp 2. *p-values are from a logistic regression model with treatment, TNFi status (IR / naïve) and CRP status ($>/\leq$ central lab ULN) as factors. **p-values are from MMRM with treatment, TNFi status (IR / naïve), CRP status ($>/\leq$ central lab ULN) and visit as factors, BL value as continuous covariate. ***Missing values were imputed as non-response. Observed data (pts) for gp 1, 2, 3, respectively: **67, 66, 62**67, 66, 63**67, 67, 65**20, 19, 20**51, 51, 50

(12.3) years (yrs), time since diagnosis was 7.4 (9.8) yrs, 57.8% male, 79.0% HLA-B27 positive, 48.6% pts had an elevated CRP 40.8% were current/ever smoker and 72.0% were TNFi-naïve. The ASAS-NSAID (SD) scores at BL were: gp 1 vs. gp 2 vs. gp 3: 82.9 (37.7) vs. 79.9 (45.3) vs. 82.3 (39.1). BASDAI and ASDAS-CRP scores were similar between groups: 6.0 (1.4) vs. 6.2 (1.5) vs. 6.2 (1.3), and 3.4 (0.7) vs. 3.3 (0.8) vs. 3.4 (0.7), respectively. The ASAS20 response at Wk 12 of pooled gp 1 and 2 vs. gp 3 was 51.1% vs. 44.3% but PE was not met (p=0.35). A higher proportion of pts in gp 1 and 2 achieved ASAS40 and BASDAI50 and other secondary outcomes at Wk 16 (Table 1). More pts in gp 1 and 2 reduced their NSAID intake from BL through Wk 16 vs. gp 3 (Table 1 and Figure 1).

Conclusion: In this population of pts with AS, SEC provided clinical improvements in conventional clinical outcomes and a short-term NSAID sparing effect.

REFERENCES:

- [1] Burmester G, et al. Ann Rheum Dis 2011;70:818-822.

Figure: Proportion of patients reaching ASAS-NSAID score=0 through Week 24

ASAS, Assessment of SpondyloArthritis international Society; NSAID, non-steroidal-anti-inflammatory drug; N, total number of pts in each treatment group; n, number of observed pts; PBO, placebo; pts, patients; SEC, secukinumab; s.c., subcutaneous; Wk, week; Data presented descriptively as observed through Wk 24; As PE failed, statistical analysis is exploratory: p-values are from a logistic regression model with treatment, TNF inhibitor status (inadequate responder / naïve) and CRP status ($>/\leq$ central lab ULN / $\leq$ lab ULN) as factors [†]p<0.001; [§]p<0.01 and [‡]p<0.05 vs group 3; Arrows indicate first application of SEC in group 1, group 2 and group 3]

Disclosure of Interests: Uta Kiltz Speakers bureau: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: Abbvie, Amgen, Biogen, Fresenius, GSK, Novartis and Pfizer, Xenofon Baraliakos Consultant of: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Jan Brandt-Juergens Speakers bureau: Abbvie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, Medac, Ulf Wagner Speakers bureau: Pfizer, Novartis and Roche, Consultant of: Pfizer, Novartis and Roche, Grant/research support from: Roche, Novartis, BMS, Pfizer, Sebastian Lieb Employee of: Novartis, Christian Sieder Employee of: Novartis, Christian Mann Employee of: Novartis, Juergen Braun Speakers bureau: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Abbvie, Amgen, Celltrion, Chugai, Medac, MSD, Novartis, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2021-eular.1033