52.7% (r-axSpA/AS: 52.6%; nr-axSpA: 52.9%) had inactive disease (ASDAS<1.3; LOCF; **Table B**). The treatment-emergent adverse event (TEAE) rate/100 patient-years' exposure was 224.2; 3.9% patients discontinued CZP due to TEAEs. No new safety signal was identified. **Conclusion:** The run-in phase of C-OPTIMISE shows that similar and substantial proportions of patients with r-axSpA/AS and nr-axSpA achieved sustained remission during 48 wks' CZP treatment. No new safety signal was identified.

Table: A) Baseline Characteristics

	axSpA (N=736) [a]	r-axSpA/AS (n=407) [b]	nr-axSpA (n=329) [b]
Age (years), mean (SD)	52.9 (7.0)	53.7 (6.8)	52.1 (7.1)
Male, n (%)	513 (69.7)	318 (78.1)	195 (59.3)
Symptom duration (years), mean (SD) [c]	2.2 (1.7)	2.5 (1.8)	1.8 (1.6)
HLA-B27 positive, n (%)	597 (81.1)	354 (87.0)	243 (73.9)
Sacroiliitis on imaging, n (%) [d]	691 (93.9)	401 (98.5)	290 (88.1)
Prior anti-TNF treatment, n (%)	31 (4.2)	20 (4.9)	11 (3.3)

B) Clinical Outcomes

	axSpA (N=736)		r-axSpA/AS (n=407)		nr-axSpA (n=329)	
%	BL	Wk48 (NRI)	BL	Wk48 (NRI)	BL	Wk48 (NRI)
ASAS20	–	79.6	–	79.9	–	79.3
ASAS40	–	72.0	–	71.3	–	72.9
ASAS-PR	–	57.3	–	55.8	–	59.3
BASDAI50	–	71.7	–	71.3	–	72.3
Mean [e]	BL	Wk48 (LOCF [e])	BL	Wk48 (LOCF [e])	BL	Wk48 (LOCF [e])
ASDAS	3.7	1.6	3.8	1.6	3.6	1.5
HDA/VHDA, %	98.5	24.7†	98.5	25.8	98.5	23.2†
ID, %	–	52.7†	–	52.6	–	52.9†
CII, % [f]	–	76.5	–	78.6	–	73.9
MI, % [f]	–	56.3	–	58.7	–	53.2
BASFI	6.7	2.1	6.7	2.1	6.7	2.2
BASFI	5.3	1.7	5.4	1.7	5.1	1.6
BASMI	3.1	2.3	3.5	2.6	2.7	1.9
Nocturnal back pain	6.9	1.8	7.0	1.8	6.8	1.8
Fatigue	7.1	2.6	7.1	2.5	7.1	2.6
CRP (mg/L), median [g]	7.8	2.0	10.7	2.0	4.5	2.0

[a] Patients with prior exposure to >1 anti-TNF excluded. [b] Central reading of patients' sacroiliac joint x-rays was used to stratify patients into r-axSpA/AS and nr-axSpA subpopulations. [c] Time since diagnosis of disease. [d] MRI or x-ray. [e] Unless stated otherwise, [f] NRI. [g] Values below the limit of quantification were set to half of the limit. 1n=734. 1n=327. AS: ankylosing spondylitis; ASAS20/40: ≥20%/40% improvement in Assessment of SpondyloArthritis International Society response criteria; ASAS-PR: ASAS Partial Remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI 50: ≥50% improvement in BASDAI; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BL: baseline; CII: ASAS Clinically Important Improvement (RFB 2.1.1); CRP: C-reactive protein; CZP: certolizumab pegol; HDA/VHDA: ASDAS High/Very High Disease Activity (ASDAS≥2.1); ID: ASDAS Inactive Disease (ASDAS<1.3); LOCF: last observation carried forward; MI: ASDAS Major Improvement (RFB 2.2.0); MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; r-axSpA: radiographic axSpA; RFB: reduction from baseline; Wk: week.

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FRI0398

IXEKIZUMAB IS EFFECTIVE IN THE TREATMENT OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS REGARDLESS OF THE LEVEL OF C-REACTIVE PROTEIN OR MAGNETIC RESONANCE IMAGING SCORES: 16-WEEK DATA FROM COAST-V AND COAST-W

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Background: Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory disease of the axial skeleton, and interleukin (IL)-17 plays an important role in the pathogenesis. Elevated C-reactive protein (CRP) levels in serum predict response to tumor necrosis factor inhibitors (TNFi)¹⁻⁴ but not to secukinumab.⁵ The role of baseline spine magnetic resonance imaging (MRI) as a predictor of response has not been investigated for IL-17 inhibitors.

Objectives: To evaluate response rates at week (wk) 16 with ixekizumab (IXE), an IL-17A antagonist, in patients with ankylosing spondylitis (AS)/r-axSpA and elevated or normal/low inflammation as measured by CRP or spinal MRI.

Methods: Two Phase 3, randomized, double-blind, placebo (PBO)-controlled trials (COAST-V, NCT02696785; COAST-W, NCT02696798) enrolled patients who were biologic-naïve or TNFi-experienced, respectively, with active disease (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥4 and spinal pain ≥4 on a numeric rating scale) and an established diagnosis of r-axSpA and fulfilling Assessment of SpondyloArthritis international Society (ASAS) criteria (sacroiliitis on radiograph by modified New York [mNY] criteria and ≥1 spondyloarthritis feature). All patients fulfilling ASAS criteria also fulfilled mNY criteria for AS. Patients were treated with IXE (80 mg every 2 or 4 wks [Q2W, Q4W]) or PBO; adalimumab (40 mg Q2W) was an active reference arm in COAST-V. We examined ASAS 40% (ASAS40) response rates at wk 16 for the intent-to-treat population by CRP (≤5 or >5 mg/L) or MRI spine inflammation (Spondyloarthritis Research Consortium of Canada [SPARCC] spine score, <2 or ≥2). Baseline spine MRI was available in 96% of patients in COAST-V and 51% of patients in COAST-W; scoring was done by central readers. Higher scores reflect greater baseline disease activity. Sacroiliac joint MRIs were not assessed. Missing data for ASAS40 were imputed by nonresponder imputation.

Results: In the COAST-V/W integrated dataset that combined biologic-naïve and TNFi-experienced populations, significantly more patients treated with IXE achieved ASAS40 response at wk 16 than with PBO in the elevated (>5 mg/L) baseline CRP group (39.3%, 42.5%, and 16.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO) and in the normal (≤5 mg/L) baseline CRP group (27.4%, 35.2%, and 12.3% for IXE Q4W, IXE Q2W and PBO, respectively; p<.05 for IXE Q4W, p<.01 for IXE Q2W vs PBO, Fig 1), and the magnitude of response with IXE between elevated vs normal CRP groups was not statistically significant. Notably, a significantly higher proportion of patients achieved ASAS40 at wk 16 with IXE than with PBO, regardless of whether MRI spine SPARCC scores were <2 (40%, 51.7%, and 15.5% for IXE Q4W, IXE Q2W and PBO, respectively; p<.01 for IXE Q4W, p<.001 for IXE Q2W vs PBO) or ≥2 (44.3%, 46.6%, and 18.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO, Fig 1).

Figure 1 COAST-V/W Integrated Dataset, ITT ASAS40 Response at Week 16, NRI

*p<.05, **p<.01, ***p<.001 versus placebo. ASAS40=Assessment in SpondyloArthritis International Society 40% response rate; CRP=C-reactive protein; ITT=Intention-to-treat; IXE=ixekizumab; NRI=nonresponder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SPARCC=Spondyloarthritis Research Consortium of Canada

Conclusion: IXE demonstrated rapid efficacy in the treatment of AS/r-axSpA at wk 16 irrespective of baseline serum CRP levels or spinal MRI score.

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FRI0399

INFLIXIMAB TROUGH LEVELS AND DISEASE ACTIVITY PREDICT EARLY CLINICAL RESPONSE IN PATIENTS WITH AXIAL SPONDYLOARTRITIS

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Background: Infliximab (Ifx) has proven to be effective in patients with axial spondyloarthritis (axSpA). Several variables may affect pharmacokinetic-pharmacodynamic of Ifx and its relation with clinical response, such as: disease activity (inflammatory burden), the development of anti-drug antibodies (ADA) and the concomitant use of conventional synthetic disease modifying anti-rheumatic drugs. The improvement of patient's management by achieving optimal serum drug concentration associated with good clinical response is the main goal of therapeutic drug monitoring (which can be helpful in the prediction of clinical response to biological treatment).

Objectives: To identify clinical and serological variables at early stages of treatment that can predict clinical response in patients with axSpA treated with Ifx.

Methods: Observational study including 81 patients with axSpA recruited from the axSpA-Paz cohort treated with Ifx and monitored during 24 weeks (W). Serum Ifx levels and ADA were measured by capture ELISA and by bridging ELISA respectively at baseline, W2, W6, W14 and W24. Disease activity was assessed at baseline and W24 by the Ankylosing Spondylitis Disease Activity Score (ASDAS) and clinical response was defined by Δ ASDAS ≥ 1.1 (clinically important improvement). The association between clinical response at W24 and clinical and serological variables was evaluated by univariable and multivariable logistic regression analyses. Serum Ifx levels at W2, 6 and 14 as a categorical variable (above or under the corresponding median value of levels at each time week), age, sex, HLA-B27, methotrexate (MTX), sulfasalazine, body mass index, smoke status, prednisone, C-reactive protein and ASDAS at baseline were included as independent variables. Receiver operating characteristic (ROC) curves for the outcome of clinical response after 24 weeks of treatment were employed to determine the best cut-off values for the predictors (serum Ifx concentrations and baseline ASDAS). Ifx survival was evaluated through Kaplan-Meier curves.

Results: In the univariable analyses, higher serum Ifx trough levels at W14 (OR: 3.9; 95%CI: 1.5-10.4); higher baseline ASDAS (OR: 1.9; 95%CI: 1.1-3.1) and MTX use (OR: 3.3; 95%CI: 1.2-8.7) were associated with a better clinical response at W24. Patients with concomitant MTX had higher serum Ifx trough levels (median and IQR) than patients without MTX and these differences were significant at W6: 26.37(16-41.4) versus 16.9(11.4-26.9); $p=0.008$; at W14: 8.4(5.4-13.9) versus 4.1(1.8-7.8); $p=0.003$ and at W22: 5.1(2.2-8.3) versus 3.1(0.6-5.4); $p=0.006$ and, respectively). In the multivariable analysis, higher ASDAS at baseline (OR: 1.8; CI 95%: 1.1-3.0) and higher serum Ifx trough levels at W14 (OR: 3.6; CI 95%: 1.3-10.4) remained significantly associated. Serum Ifx concentration at W14 ≥ 6.7 μ g/mL and a disease activity score at baseline ≥ 3.5 were found to be associated with higher Δ ASDAS at W24 (OR: 16; 95%CI: 3.6-71.7). No patient with Ifx levels at W14 ≥ 6.7 μ g/mL developed ADA during the 24 weeks follow up. The combination of both variables was used to predict clinical response with a sensitivity of 87.5%, specificity of 69.6%, PPV of 75% and NPV of 84.2%.

Conclusion: Elevated baseline ASDAS and high serum Ifx trough levels at W14 are associated with better clinical response at 24 weeks in patients with axSpA under Ifx therapy. A predictive model based on these variables is suggested to identify early responders to Ifx treatment.

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FRI0400

LONG-TERM SAFETY OF IXEKIZUMAB IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTRITIS/ ANKYLOSING SPONDYLITIS: AN INTEGRATED ANALYSIS OF COAST-V AND COAST-W

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Background: The efficacy and safety of ixekizumab (IXE) in patients with radiographic axial spondyloarthritis (r-axSpA) were investigated in the COAST trial program.

Objectives: To report the long-term safety of IXE in r-axSpA patients using integrated safety data from the COAST trials program.

Methods: Safety data for r-axSpA patients treated with IXE were integrated from COAST-V (biologic-naïve; NCT02696785) and COAST-W (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT02696798) studies. Patients fulfilled ASAS criteria for r-axSpA and mNY criteria for ankylosing spondylitis. Trial eligibility criteria were previously reported.^{1,2} In these studies, participants were randomized to placebo (n=191), adalimumab (n=90, active reference arm, COAST-V only), or ixekizumab (n=376). Study participants initially randomized to IXE in both trials were treated with a starting dose (80-mg or 160-mg) and then 80-mg IXE every 2 weeks (IXEQ2W) or 4 weeks (IXEQ4W). Patients initially treated with placebo or adalimumab were re-randomized at Week 16 to receive either IXEQ2W or IXEQ4W following a 160-mg starting dose. The analysis population included all ixekizumab-exposed patients in both trials. Incidence rates (IR) per 100 person years with 95% confidence intervals (CI) and the number of patients are reported. Adverse Event (AE) codes were derived from MedDRA (v21.0). Integrated safety data presented here include all data collected between May 6, 2016 and Sept. 20, 2018.

Results: The integrated population consisted of 641 patients with 749.6 total patient-years of exposure to IXE. Mean follow up time was 427 days. Mean baseline age was 43.8 $\pm$ 12.3 years. Mean and median baseline disease symptom duration (since onset) were 17.2 $\pm$ 10.8 years and 15.5 years (Min: 1.1, Max: 56.2), respectively. Safety data are presented in Table 1. Among these patients, 489 (76.3%) reported ≥ 1 treatment