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.

REFERENCES:

[1] Inman, et al. 2008
[2] Braun, et al. 2016
[3] de Vries, et al. 2009
[4] Vastesaeger, et al. 2011
[5] Braun, et al. 2018

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FRI0399 INFLIXIMAB TROUGH LEVELS AND DISEASE ACTIVITY PREDICT EARLY CLINICAL RESPONSE IN PATIENTS WITH AXIAL SPONDYLOARHTRITIS

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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 ΔASDAS$\geq$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 o 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 $\geq$ 6.7 µg/mL and a disease activity score at baseline $\geq$ 3.5 were found to be associated with higher ΔASDAS at W24 (OR: 16; 95%CI: 3.6-71.7). No patient with Ifx levels at W14 $\geq$ 6.7 µg/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 SPONDYLOARTHRITIS/ 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±12.3 years. Mean and median baseline disease symptom duration (since onset) were 17.2±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 $\geq$1 treatment

emergent AEs with an IR of 65.2. Serious AEs (≥1) were reported for 51 (8.0%) patients with an IR of 6.8. Discontinuations due to AEs were reported for 38 (5.9%) patients with an IR of 5.1. One death was reported, a suicide, in a patient with a documented prior history of depression and judged by the blinded principal investigator to be unrelated to the investigational product. The overall infection IR was 39.4, with both serious and opportunistic infections reported with an IR of 1.7. Among opportunistic infections, no *Tuberculosis* infections or reactivations were reported and the *Candida* infection IR was 1.2. No infections were associated with grade 3 or 4 neutropenia. The confirmed major adverse cardiovascular events IR was 0.1. The malignancy IR was 0.4 with acute promyelocytic leukemia, bladder cancer, and ovarian cancer reported. The depression IR was 0.8. The adjudicated inflammatory bowel disease (IBD) IR was 1.5 with 4 of 11 patients having prior history of IBD. The Anterior uveitis (AU) IR was 3.9 with 24 of 29 patients having prior history of AU. The injection site reaction IR was 11.3.

Table 1. Integrated Safety Outcomes

	n (%)	IR (CI)
Treatment Emergent AEs	489 (76.3%)	65.2 (59.7, 71.3)
Serious AEs	51 (8.0%)	6.8 (5.2, 9.0)
Discontinuation due to AEs	38 (5.9%)	5.1 (3.7, 7.0)
Death	1 (0.2%)	0.1 (0.0, 0.9)
Infections[a]	295 (46.0%)	39.4 (35.1, 44.1)
Serious Infections	13 (2.0%)	1.7 (1.0, 3.0)
Opportunistic Infections	13 (2.0%)	1.7 (1.0, 3.0)
Candida	9 (1.4%)	1.2 (0.6, 2.3)
Tuberculosis	0	0
Confirmed MACE	1 (0.2%)	0.1 (0.0, 0.9)
Malignancies	3 (0.5%)	0.4 (0.1, 1.2)
Depression	6 (0.9%)	0.8 (0.4, 1.8)
Adjudicated IBD	11 (1.7%)	1.5 (0.8, 2.6)
Anterior Uveitis	29 (4.5%)	3.9 (2.7, 5.6)
Injection Site Reactions	85 (13.3%)	11.3 (9.2, 14.0)

[a]Infections reported with frequencies ≥2.5% included nasopharyngitis (12.2%), upper respiratory tract infection (10.9%), pharyngitis (4.2%), bronchitis (3.6%), urinary tract infection (2.7%), and gastroenteritis (2.5%).

MACE, major adverse cardiovascular events; IBD, inflammatory bowel disease; AE, adverse event; n, number of patients; IR, incidence rate; CI, 95% confidence interval

Conclusion: The reported safety profile for IXE in r-axSpA is consistent with the profile reported for other indications. During the extension period, the overall safety profile of ixekizumab remained consistent with that observed during the double-blind period of COAST-V and COAST-W.[1,2]

REFERENCES:

[1] [Van der Heijde et al Lancet 2018 2Deodhar et al Arthritis Rheumatol 2018]

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FRI0401 EFFECT OF LONG-TERM TREATMENT WITH SECUKINUMAB ON LIPID PROFILE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: POOLED 4 YEAR ANALYSIS

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Background: Systemic inflammation may adversely affect the lipid profile in AS and PsA patients (pts)[1]. Treatment with some TNF and JAK inhibitors have reported increased total cholesterol (TC) and triglycerides (TG) despite reduction in inflammation[2-3]. Secukinumab (SEC), a fully human monoclonal antibody that directly inhibits IL-17A, has demonstrated a sustained efficacy and consistent safety profile in pts with AS and PsA[4]

Objectives: To evaluate the long-term effect of SEC on key lipid parameters in AS and PsA pts from pooled phase 3 clinical trials, through 208 weeks (wks)

Methods: This *post hoc* analysis included pooled data from MEASURE 1-4 (SEC 150 mg) in AS (N = 892) and FUTURE 2-5 studies (SEC 150/300 mg) in PsA (N = 2049), from pts treated with SEC or placebo (PBO). Serum TC, TG, LDL- and HDL-cholesterol and TC/HDL-C levels were assessed at baseline (BL), Wks 16, 104 and 208 in overall population and in sub-groups by prior anti-TNF therapy, concomitant methotrexate (MTX) and BL statin usage. Shift of common terminology criteria for adverse events (CTCAE) grade from BL through Wk 208 were also analysed

Results: BL characteristics were comparable across SEC and PBO groups. Lipid levels were stable in SEC treated AS and PsA pts through Wk 208 (**Table**) with mean change (mmol/L) from BL in AS: TC = ±0.1, TG = 0.1-0.2, LDL-C = ±0.1, HDL-C = ±0.04 and TC/HDL-C = ±0.2 and PsA: TC = ±0.2, TG = 0.001-0.2, LDL-C = ±0.2, HDL-C = ±0.06 and TC/HDL-C = ±0.2. Stable lipid values were also seen across key subgroups by prior anti-TNF therapy, concomitant MTX and BL statin usage, which remained stable through Wk 208. No Change in CTCAE lipid grades was observed in >90% of SEC-treated pts through Wk 208

Conclusion: SEC did not adversely affect the lipid profile and TC/HDL-C ratio in pts with AS and PsA, over 4 years. The lipid profile remained stable with SEC treatment and was sustained irrespective of prior anti-TNF status, concomitant MTX and BL statin usage

REFERENCES:

[1] Papagoras C, et al. Joint Bone Spine 2014;81:57-63
[2] Wolk R, et al. J Clin Lipidol.. 2017;11:1243-56
[3] Agca R, et al. J Rheumatol. 2017; 44(9):1362-8
[4] Lubrano E and Perrotta FM. Ther Clin Risk Manag. 2016;12:1587-92

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