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

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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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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 $\pm$ 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