Spinal Radiographic Progression and Predictors of Progression in Patients With Radiographic Axial Spondyloarthritis Receiving Ixekizumab Over 2 Years

Désirée van der Heijde, Mikkel Østergaard, John D. Reveille, Xenofon Baraliakos, Andris Kronbergs, David M. Sandoval, Xiaoqi Li, Hilde Carlier, David H. Adams, Walter P. Maksymowycz

The Journal of Rheumatology. https://doi.org/10.3899/jrheum.210471

Hello, I’m Dr Walter Maksymowycz, a Professor of Medicine at the University of Alberta. I would like to share with you the key highlights from the analysis of radiographic progression in patients with radiographic axial spondyloarthritis receiving ixekizumab.¹

Radiographic axial spondyloarthritis is a chronic inflammatory disease of the axial skeleton, where patients have radiographically defined grade 3 or 4 unilateral, or at least grade 2 bilateral structural damage, per modified New York criteria, at the sacroiliac joint.¹² As the disease advances, excessive new bone formation may lead to irreversible ankylosis in the spine resulting in functional deterioration.¹ This analysis aimed to evaluate the effects of ixekizumab, an approved interleukin-17 inhibitor for the treatment of radiographic axSpA, on radiographic changes in the spine in patients with radiographic axSpA, by measuring change from baseline through 2 years in the modified Stoke Ankylosing Spondylitis Spinal Score, or mSASSS.¹³⁻⁴ The analysis also aimed to identify potential predictors of progression.¹

For patients with radiographic axSpA, the mSASSS is a validated and widely used assessment that evaluates the severity of structural damage and progression of radiographic changes.⁵ The mSASSS requires lateral radiographs of the lumbar and cervical vertebrae, and scores each upper and lower anterior vertebral corner from 0 indicating no abnormality, to 3 indicating total bony bridging.⁵⁻⁶ Across the 24 vertebral corners the mSASSS total score ranges from 0 to 72.⁵⁻⁶

This analysis included patients with radiographic axSpA who were bioDMARD-naïve from COAST-V, and TNFi-experienced patients from COAST-W, who initially received ixekizumab every 2 weeks or every 4 weeks and continued the same ixekizumab dosing regimen for 2 years.¹ Lateral view radiographs of cervical and lumbar spine were performed at baseline and 2 years post-baseline and scored using the mSASSS scoring system.¹ Predictors of spinal progression were identified in logistic regression models, initially in a univariate analysis of variables of interest, and subsequently using a multivariate analysis to select variables for the final prediction model.¹

The patient characteristics were as expected for a radiographic axSpA population, including patients who were predominantly male, HLA-B27-positive, with a mean symptom duration at baseline of approximately 16 years.¹ Patient characteristics were similar between ixekizumab dose groups, where mean baseline mSASSS score was 11, and approximately 40% of evaluable patients had syndesmophytes at baseline.¹
The mean change in mSASSS from baseline at Year 2 was 0.4 and 0.3 for the ixekizumab every 4 weeks and Total ixekizumab groups, respectively. Based on a definition of non-progression, defined as an mSASSS change from baseline of less than 2, 88.7% of patients treated with ixekizumab every 4 weeks and 89.6% of all patients treated with ixekizumab were non-progressors through 2 years of treatment. Change in mSASSS was numerically higher for patients with the following characteristics: at least 40 years of age, males, the presence of syndesmophytes at baseline, HLA-B27-positive status, baseline Ankylosing Spondylitis Disease Activity Score of greater than 3.5, and Week 16 and 52 Spondyloarthritis Research Consortium of Canada, or SPARCC, magnetic resonance imaging spine score of greater than 2. For evaluable patients in the ixekizumab every 4 weeks and Total ixekizumab groups, 93% and 95.2%, respectively, did not develop syndesmophytes through 2 years of treatment with ixekizumab. Where MRI measures were available at baseline and Week 52 for the COAST-V population, the predictor of structural progression at Year 2 (defined as a change in total mSASSS >0 and ≥2) was Week 52 inflammation in SPARCC spine score ≥2.

In conclusion, the majority of patients with radiographic axSpA receiving ixekizumab for 2 years had no radiographic progression in the spine and the overall mean progression was low. The potential predictors of progression were generally consistent with previous observations, and included age, presence of syndesmophytes at baseline, HLA-B27 status, and male gender. The finding that persistent MRI inflammation is associated with radiographic progression is a novel observation that requires further study in other cohorts.

References