POS0918

EVALUATION OF SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS RECEIVING IXEKIZUMAB THERAPY OVER 2 YEARS

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Background: It is important to understand the potential effect long-term therapy with biologics can have on structural changes in the spine among patients with active radiographic axial spondyloarthritis (r-axSpA, ankylosing spondylitis).

Objectives: We examined radiographic progression in the spine among patients with active r-axSpA treated with ixekizumab, an IL-17A antagonist, for 2 years, and potential predictors of spinal radiographic progression.

Methods: Patients with active r-axSpA, biologic-naïve (COAST-V, NCT02696785) or with prior experience with a maximum of 2 TNF inhibitors (COAST-W, NCT02696798), received 80mg ixekizumab every 2 or 4 weeks for 2 years (108 weeks, of which 56 weeks were the COAST-Y extension study, NCT03129100). Mean change from baseline of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) (average score from 2 selected readers, blinded for time order) for patients treated with ixekizumab for 2 years with data at both baseline and year 2 is presented (N=230; 54% of total randomized patients). Non-progression is presented for all patients and subgroups based on TNFi-experience. Predictors were identified in multivariate logistic regression models with stepwise selection criteria of p-value <0.1. All data are observed.

Results: At baseline, patients (N=230) were predominately male (82%) with an average age of 43 years, mean symptom duration of 16 years, 52% were TNFi-experienced, mean (SD) ASDAS score was 4.0 (0.7), most were HLA-B27 positive (87%) and 40% had syndesmophytes (identified by both selected readers at the same location). Baseline mSASSS (SD) was 11.0 (16.3) and change from baseline at year 2 of treatment was 0.3 (1.8) (Table 1). The proportion of non-progressors (mSASSS change from baseline <2) over 2 years was 89.6% (total IXE [all patients]), 90.9% (biologic-naïve) and 88.3% (TNFi-experienced), and, if defined as mSASSS change from baseline ≤0, 75.7% (total IXE [all patients]), 78.2% (biologic-naïve) and 73.3% (TNFi-experienced) (Table 1). Predictors of structural progression at year 2 (mSASSS change >0) were age, baseline syndesmophytes, HLA-B27 status and gender (Table 1). Week 52 inflammation in MRI SPARCC spine was also identified as a predictor for structural progression at year 2 in a separate model for patients from COAST-V where MRI measures were available at baseline and Week 52 (N=109).

Conclusion: The majority of patients treated with ixekizumab for 2 years did not show radiographic progression, and the overall mean progression was low. Similar levels of non-progression were observed in biologic-naïve patients and patients previously exposed to TNFis. Predictors were generally consistent with previous studies.

Table 1. Spinal radiographic changes for patients with active r-axSpA treated with ixekizumab for 2 years

Change in mSASSS at year 2	All patients ^a N=230	Biologic-naïve N=110	TNFi-experienced N=120
Baseline mSASSS, mean (SD)	11.0 (16.3)	10.1 (15.5)	11.7 (17.0)
Change at year 2, mean (SD)	0.3 (1.8)	0.3 (2.0)	0.4 (1.6)
Change in total mSASSS <2, n (%)	206 (89.6)	100 (90.9)	106 (88.3)
Change in total mSASSS ≤0, n (%)	174 (75.7)	86 (78.2)	88 (73.3)
Multivariable logistic regression model			
Prediction for change in total mSASSS >0, OR (95% CI), p-value			
All patients^{a,b}			
	N=228		
Age (≥40 years vs. <40 years)	2.97 (1.41, 6.28)		p=0.004 ^c
Baseline syndesmophytes ^b (yes vs. no)	2.31 (1.18, 4.54)		p=0.015 ^c
Baseline HLA-B27 (positive vs. negative)	3.78 (1.04, 13.75)		p=0.044 ^c
Gender (male vs. female)	3.16 (1.01, 9.86)		p=0.047 ^c
Baseline ASDAS state (>3.5 vs. [2.1, 3.5])	2.26 (0.96, 5.34)		p=0.063

^aCombined ixekizumab group of Q2W and Q4W patients with baseline and year-2 mSASSS data^bIdentified by both selected readers at the same location (2 patients were not evaluable by both readers)^cp<0.05Abbreviations: ASDAS=Assessment of Disease Activity, CI=confidence interval, IXE=ixekizumab, mSASSS=modified Stoke Ankylosing Spondylitis Spinal Score, OR=odds ratio, Q2W=every 2 weeks, Q4W=every 4 weeks, SD=standard deviation, TNFi=tumor necrosis factor inhibitor

Disclosure of Interests: Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Employee of: Director of Imaging Rheumatology bv., Mikkel Østergaard Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly and Company, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, Grant/research support from: AbbVie, BMS, Merck, UCB, Celgene, Novartis, John D Reville Paid instructor for: UCB, Eli Lilly and Company, Consultant of: UCB, Eli Lilly and Company, Pfizer, Novartis, Grant/research support from: Janssen, Eli Lilly and Company, Xenofon Baraliakos Speakers bureau: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Paid instructor for: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Consultant of: Abbvie, BMS, Lilly, Janssen, Novartis, MSD, Pfizer, Galapagos, Gilead, UCB, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Xiaoqi Li Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Hilde Carlier Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Walter P Maksymowych Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Boehringer, BMS, Eli Lilly and Company, Novartis, Pfizer, UCB, Grant/research support from: Abbvie, Novartis, Pfizer

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BIMEKIZUMAB SHOWS SUSTAINED LONG-TERM IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES AND QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A PHASE 2B STUDY

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Background: Bimekizumab (BKZ), a monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy and safety in patients with ankylosing spondylitis (AS) treated over a period up to 96 weeks.^{1,2}

Objectives: To report 3-year interim patient-reported outcomes (PROs) in patients with active AS treated with BKZ in a phase 2b dose-ranging study (BE AGILE; NCT02963506) and its open-label extension (OLE; NCT03355573).

Methods: BE AGILE study design has been described previously.¹ Patients treated with BKZ 160 mg or 320 mg every 4 weeks (Q4W) at Week 48 in BE AGILE were eligible for OLE entry. All OLE patients received BKZ 160 mg Q4W. Outcome measures are reported for the OLE full analysis set (patients who entered the OLE and had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement in the OLE), and include: BASDAI, BASDAI50 responder rate, BASFI, fatigue (BASDAI Q1), morning stiffness (mean of BASDAI Q5+6), total spinal pain (numeric rating scale [NRS]), SF-36 PCS and MCS, and ASQoL. Missing data were imputed using multiple imputation (MI; based on the missing at random assumption) for continuous variables and non-responder imputation (NRI) for dichotomous variables.

Results: 262/303 (86%) patients randomised at BE AGILE study baseline (BL) completed Week 48 on BKZ 160 mg or 320 mg, of whom 255/262 (97%) entered the OLE (full analysis set: 254). From baseline to Week 48 in BE AGILE, BKZ-treated patients showed clinically relevant improvements in disease activity (BASDAI, BASDAI50), physical function (BASFI), fatigue, morning stiffness, spinal pain, and quality of life (SF-36 PCS and MCS, ASQoL) (Figure 1). Group-level improvements in all reported continuous efficacy measures exceeded published minimally important difference (MID), minimum clinically important improvement (MCII), and/or minimum clinically important difference (MCID) thresholds (Figure 1).^{3,4} Efficacy in all reported outcome measures was maintained or continued to improve from Week 48 to Week 144 or 156 (Figure 1).

Conclusion: BKZ treatment was associated with sustained and consistent efficacy in patients with active AS over 3 years, including patient-reported disease activity, physical function, fatigue, morning stiffness, spinal pain, and quality of life.