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POS0908

EFFICACY OF IXEKIZUMAB THROUGH 52 WEEKS FOR IMPROVING PERIPHERAL JOINT INVOLVEMENT AMONG PATIENTS WITH RADIOGRAPHIC-AXIAL SPONDYLOARTHRITIS

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Background: Radiographic-axial spondyloarthritis (r-axSpA) is a progressive chronic inflammatory disease primarily affecting the spine and sacroiliac joints. However, about 30-40% of patients (pts) with axSpA can have peripheral joint involvement, including joint tenderness and swelling, which can contribute significantly to burden of disease. Ixekizumab (IXE), a monoclonal antibody that neutralizes the pro-inflammatory cytokine interleukin-17A, has demonstrated a high level of efficacy in the treatment of r-axSpA.

Objectives: The aim of this study is to evaluate the efficacy of IXE through 52 weeks (wks) in improving peripheral joint pain and swelling for pts with r-axSpA.

Methods: Data was derived from two phase III randomised, double-blind, placebo (PBO)-controlled trials: one in pts with r-axSpA, who were biological disease-modifying anti-rheumatic drug (bDMARD)-naïve (COAST-V: NCT02696785), and the other in pts who were tumor necrosis factor inhibitor-experienced (COAST-W: NCT02696798). All pts had a confirmed diagnosis of r-axSpA and had to meet ASAS (Assessment of SpondyloArthritis international Society) criteria. IXE (80 mg) or PBO were administered subcutaneously every 2 (Q2W) or 4 (Q4W) wks during a 52-wk treatment period, after receiving a starting dose of 80 mg or 160 mg at wk 0. COAST-V/W pts originally randomised to PBO were re-randomised 1:1 to IXE Q4W or Q2W at wk 16. We present a post-hoc analysis of data from an integrated dataset from COAST-V and W (COAST-V/W); with intent to treat (ITT) pts categorized by baseline (BL) peripheral joint status. The presence of peripheral joint involvement was defined using a 46-joint tender joint count (TJC) >0 or 44-joint swollen joint count (SJC) >0. Treatment response through wk 52 was evaluated based on % improvement (20%, 50% or 70%) and resolution of tender or swollen joints of pts with BL TJC>0 or SJC>0, respectively. Missing data were imputed by non-responder imputation (NRI). Treatment comparison vs PBO at wk 16 was performed using Cochran-Mantel-Haenszel test.

Results: This analysis includes 359 pts (63.4% of ITT) with baseline TJC>0 and 203 pts (35.9% ITT) with baseline SJC>0. The mean (SD) baseline TJC and SJC were 7.7 (8.3) and 4.3 (4.5), respectively. Mean BL TJC and SJC values by treatment group are presented in Table 1. A significant improvement of SJC by 20% and 50% was seen in pts treated with IXE Q4W compared to PBO at wk 16. Pts treated with IXE resulted in a numerically higher improvement in TJC and SJC symptoms up to wk 16 compared to PBO, and efficacy was sustained up to wk 52 (Table 1). A higher proportion of IXE-treated pts achieved high-hurdle efficacy endpoints (50% and 70% improvements) in comparison to PBO at wk 16 (Table 1). Over this time period, IXE treatment led to a high proportion of pts experiencing complete resolution of TJC or SJC vs PBO at wk 16, which was sustained up to wk 52 (Fig 1).

Conclusion: In this post hoc analysis, pts with r-axSpA treated with IXE showed substantial improvement in peripheral joint pain and swelling.

Table 1. Improvement of Tender or Swollen Joint Counts for pts with radiographic-axSpA with TJC>0 or SJC>0 at baseline (COAST-V/W)^a - NRI Results

% Improvement	Wk	Radiographic-AxSpA				
		16		52 ^b		
		PBO	IXE Q4W	IXE Q2W	IXE Q4W	IXE Q2W
N (TJC>0)		116	129	114	129	114
BL TJC mean (SD)		7.4 (8.8)	8.4 (8.4)	7.3 (7.5)		
%TJC improvement	20%	66.4	75.2	71.1	68.2	72.8
	50%	52.6	61.2	64.9*	65.1	67.5
	70%	37.9	47.3	50	55.8	54.4
N (SJC>0)		67	72	64	72	64
BL SJC mean (SD)		3.8 (4.6)	5.2 (5.2)	3.8 (3.3)		
%SJC improvement	20%	64.2	83.3*	76.6	77.8	78.1
	50%	56.7	77.8†	70.3	75	76.6
	70%	46.3	62.5	60.9	69.4	71.9

Abbreviations: COAST-V/W= integrated COAST-V and COAST-W; PBO = placebo; IXE= ixekizumab; Q4W = 80 mg IXE every 4 wks; Q2W = 80 mg IXE every 2 wks^aImprovement in the number of tender or swollen joints were summarized on ITT patients who had tender (TJC>0) or swollen (SJC>0) joints at baseline, respectively^bCOAST-V/W PBO data are not available at wk 52 as pts originally randomised to PBO were re-randomised 1:1 to IXE Q4W or IXE Q2W at wk 16p-value vs. PBO at wk 16: *P<0.05, †P<0.01, ‡P<0.001

Figure 1. Complete Resolution of Tender or Swollen Joint Counts for pts with radiographic-axSpA with TJC>0 or SJC>0 at baseline (COAST-V/W) ^a - NRI Results

Figure Legend
Abbreviations: COAST-V/W= integrated COAST-V and COAST-W; PBO = placebo; IXE= ixekizumab; Q4W = 80 mg IXE every 4 wks; Q2W = 80 mg IXE every 2 wks

^aComplete Resolution in the number of tender or swollen joints were summarized on ITT patients who had tender (TJC>0) or swollen (SJC>0) joints at baseline, respectively

^bCOAST-V/W PBO data are not available at wk 52 as patients originally randomised to PBO were re-randomised 1:1 to IXE Q4W or IXE Q2W at wk 16
p-value vs. PBO at wk 16: *P<0.05, †P<0.01, ‡P<0.001

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POS0909

IXEKIZUMAB IMPROVES SIGNS, SYMPTOMS AND QUALITY OF LIFE OF ANKYLOSING SPONDYLITIS IN PATIENTS IRRESPECTIVE OF HLA-B27 STATUS: POOLED RESULTS FROM THE COAST-V AND COAST-W TRIALS

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Background: Human leukocyte antigen-B27 (HLA-B27) is found in most patients (pts) with ankylosing spondylitis (AS). Although a subset of pts with AS are HLA-B27 negative (NEG), ensuring treatment efficacy in this subpopulation is important.

Objectives: This analysis evaluated the efficacy of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, in AS pts who are either HLA-B27 positive (POS) or NEG.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were 2 phase 3, multicenter, randomized, double-blind, PBO-controlled trials investigating the efficacy of 80-mg IXE administered every 4 weeks (Q4W) and every 2 weeks (Q2W) in pts naïve to biological disease-modifying anti-rheumatic drugs (bDMARDs; COAST-V) and in those who were inadequate responders or intolerant to 1 or 2 tumor necrosis factor inhibitors (TNFi; COAST-W). Only data from pts randomized at baseline to PBO, IXE Q4W or Q2W in both trials who met per protocol eligibility criteria were integrated and stratified based on HLA-B27 status (POS, NEG) for an *ad hoc* subgroup analysis. Efficacy was assessed using the Assessment of Spondyloarthritis International Society 40 (ASAS40), Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) and Short Form 36 Physical Component Scores (SF-36 PCS). Missing data were imputed by non-responder imputation (NRI) for binary measure and by modified baseline observation carried forward (mBOCF). Data from PBO was reported up to Week 16 and for pooled IXE Q4W and Q2W up to Week 52.

Results: This analysis includes pts with AS who are HLA-B27 POS (N=453; PBO=155, IXE=298) or NEG (N=62, PBO=21, IXE=41). Overall, more pts were male (82.6%, POS; 77.4%, NEG), and for IXE treated pts, the duration of disease since r-axSpA diagnosis was 10.3 (SD=9.1) and 6.9 (SD=5.6) years, among POS and NEG pts respectively (Table 1). Among IXE treated patients,

Table 1. Baseline Characteristics by HLA-B27 Positive and Negative Status

	Positive HLA-B27		Negative HLA-B27	
	PBO (N=155)	IXE (N=298)	PBO (N=21)	IXE (N=41)
Male, n (%)	133 (85.8)	241 (80.9)	18 (85.7)	30 (73.2)
Age of r-axSpA onset (yr), mean (SD)	25.2 (9.28)	26.3 (8.38)	35.4 (8.43) [‡]	34.6 (10.32) [‡]
Duration of symptoms since r-axSpA onset (yr)	18.7 (11.82)	17.1 (10.38)	16.0 (9.69)	15.9 (12.40)
C-Reactive protein (mg/L), mean (SD)	16.7 (22.43)	16.9 (25.50)	18.1 (21.69)	13.7 (14.38)
ASDAS score, mean (SD)	4.0 (0.78)	4.0 (0.83)	4.3 (0.76)	4.1 (0.73)
BASDAI score, mean (SD)	7.1 (1.25)	7.2 (1.37)	7.6 (1.31) [*]	7.4 (1.41)
SF-36 PCS, mean (SD)	33.7 (7.50)	33.2 (7.63)	34.1 (8.28)	31.4 (7.67)

Abbreviations: ASDAS, Assessment of Spondyloarthritis International Society 40; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; N, total number of patients in group; n, number of patients in category/subgroup; PBO, placebo; r-axSpA, axial spondyloarthritis; SD, standard deviation; SF-36 PCS, Short Form 36 Physical Component Scores; yr, years. ^{*}p-value: vs. HLA-B27 positive; [‡]p < 0.001

the mean age of HLA-B27 NEG pts was approximately 7-8 years older than HLA-B27 POS pts. At Week 16, 39.6% (n=118/298) of HLA-B27 POS and 29.3% (n=12/41) of HLA-B27 NEG pts achieved ASAS40, and 34.6% (n=103) of HLA-B27 POS and 17.1% (n=7) of HLA-B27 NEG pts achieved BASDAI50; improvements were seen as early as Week 1 and sustained or improved up to Week 52. The mean baseline SF-36 PCS was 33.2 (SD=7.63) for HLA-B27 POS and 31.4 (SD=7.67) for HLA-B27 NEG pts. At Week 16, the mean change from baseline in SF-36 PCS was 7.3 (SD 7.6) for HLA-B27 POS and 3.7 (SD=6.83) for HLA-B27 NEG pts. Improvements were sustained to Week 52 (Figure 1).

Conclusion: IXE improves signs, symptoms, patient-reported outcomes and health-related quality of life in HLA-B27 POS and NEG pts with AS, however the HLA-B27 POS pts have a faster and more robust response than HLA-B27 NEG pts.

Figure 1. Proportion of patients achieving ASAS40 by HLA-B27 Positive and Negative Status in patients randomized to placebo up to Week 16 and ixekizumab up to Week 52

Abbreviations: ASAS40, Assessment of Spondyloarthritis International Society 40; HLA-B27, Human leukocyte antigen-B27; IXE, pooled ixekizumab every 2 weeks and every 4 weeks; NRI, nonresponder imputation

Figure 1. Comparisons done using t-test and chi-square test for continuous and categorical variables.

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POS0910

EVALUATION OF THE NONSTEROIDAL ANTI-INFLAMMATORY DRUG-SPARING EFFECT OF SECUKINUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS OF THE MULTICENTER, RANDOMISED, DOUBLE-BLIND, PHASE IV ASTRUM-TRIAL

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