AB0744

EFFICACY OF IXEKIZUMAB IN ACTIVE PSORIATIC ARTHRITIS (PSA) PATIENTS WITH AXIAL PAIN STARTING BEFORE AGE 45: A SUBGROUP ANALYSIS OF SPIRIT-P1 AND SPIRIT-P2 PHASE 3 CLINICAL TRIALS

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Background: The efficacy and safety of ixekizumab (IXE), an IL-17A antagonist, was investigated in patients with active psoriatic arthritis (PsA) in the SPIRIT-P1 and SPIRIT-P2 clinical trials.

Objectives: To investigate the efficacy of ixekizumab on axial pain, fatigue, stiffness, and physical function in a subset of patients with PsA self-reporting axial pain starting before the age of 45 years at baseline.

Methods: Patients with PsA in the intent-to-treat populations of SPIRIT-P1 (Biologic-naïve; NCT01695239) and SPIRIT-P2 (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT02349295) with baseline patient-reported axial pain (≥ 4 Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] question 2), high-sensitivity C-reactive protein (hsCRP) $>5\text{mg/L}$, and <45 years old were included in this post-hoc integrated analysis. SPIRIT-P1/P2 did not include axial imaging. Patients were treated with placebo (PBO) or ixekizumab 80-mg every 2 weeks (IXEQ2W) or 4 weeks (IXEQ4W) after a 160-mg starting dose for 24 weeks. The efficacy of ixekizumab on axial pain (BASDAI question 2), fatigue (BASDAI question 1), stiffness (mean of BASDAI questions 5/6), total BASDAI, Health Assessment Questionnaire Disability Index (HAQ-DI), and 36-Item Short Form Health Survey Physical Component Summary (SF-36 PCS) was analyzed at Weeks 16 and 24 using mixed model for repeated measures with treatment, region, baseline conventional DMARD experience, visit, and treatment-by-visit interaction as fixed factors, and response value at baseline as a covariate.

Results: Axial pain and stiffness significantly improved at Weeks 16 and 24 in patients with PsA treated with IXEQ4W or IXEQ2W versus PBO ($p<0.05$; Table 1). Fatigue significantly improved at Week 16 in patients treated with IXEQ4W or IXEQ2W versus PBO and at Week 24 with IXEQ2W versus PBO ($p<0.05$). Total BASDAI scores significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO ($p<0.01$). Physical function significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO when assessed by HAQ-DI or SF-36 PCS ($p<0.05$).

	PBO N=32		IXEQ4W N=36		IXEQ2W N=37	
	Week 16 n=28	Week 24 n=13	Week 16 n=36	Week 24 n=29	Week 16 n=37	Week 24 n=33
BASDAI total	-0.78±0.51	-1.29±0.56	-2.80±0.45†	-3.28±0.45†	-3.32±0.47‡	-3.53±0.47‡
Question 1 (Fatigue)	-0.53±0.49	-1.07±0.56	-1.84±0.43*	-2.17±0.44	-2.52±0.46‡	-2.72±0.46†
Question 2 (Axial Pain)	-1.26±0.55	-1.85±0.61	-3.25±0.48†	-3.53±0.47*	-3.19±0.49†	-3.45±0.48*
Questions 5/6 (Stiffness)	-0.32±0.58	-0.86±0.65	-2.40±0.50†	-3.09±0.52†	-3.01±0.51‡	-3.16±0.52‡
HAQ-DI	-0.02±0.13	-0.15±0.13	-0.40±0.12†	-0.52±0.12*	-0.52±0.11‡	-0.51±0.11*
SF-36 PCS	1.53±5.15	3.64±5.44	15.56±4.73*	22.38±4.71†	18.33±4.77†	17.26±4.71*

* $p<0.05$, † $p<0.01$, ‡ $p<0.001$, all vs. PBO.

Conclusion: Ixekizumab treatment yielded significantly higher improvements than placebo in axial pain, fatigue, stiffness, and physical function at Weeks 16 and 24 in the integrated PsA subpopulation self-reporting axial pain at baseline. These analyses were limited by a lack of baseline axial imaging.

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AB0745

ASSESSMENT OF DISEASE ACTIVITY USING RAPID3 AND EVALUATION OF TREATMENT EFFECT OF GUSELKUMAB IN PATIENTS WITH PSA: RESULTS FROM A RANDOMIZED PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL

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Background:

Objectives: To evaluate the effect of guselkumab (GUS) on Routine Assessment of Patient Index Data 3 (RAPID3) in patients with psoriatic arthritis (PsA).

Methods: In a phase 2 trial, patients with active PsA and $\geq 3\%$ body surface area of plaque psoriasis despite current or previous treatment with standard-of-care therapies, including anti-TNF α agents, were randomized 2:1 to receive GUS 100 mg (n=100) or placebo (PBO, n=49) subcutaneously at wks 0, 4, and every 8 wks (q8w) thereafter through wk44. At wk16, patients from either group with $<5\%$ improvement from baseline in both swollen and tender joint counts were eligible for early escape to open-label ustekinumab. At wk24, all remaining PBO patients crossed-over to receive GUS 100 mg, and then received GUS at wk28 and q8w thereafter through wk44. RAPID3 (0-30) is derived from the Multi-Dimensional Health Assessment Questionnaire (MDHAQ) and numerical rating scales (0-10) for pain and patient global assessment. A change of 5.1 in RAPID3 score was identified as the minimally important difference (MID) in PsA, and RAPID3 ≤ 3.0 was used to define PsA remission. Change in RAPID3 and proportion of patients achieving MID were compared between treatments. Correlations of RAPID3 scores with the PsA Disease Activity Score (PASDAS), GRACE index, Disease Activity in Psoriatic Arthritis (DAPSA), and Modified Composite Psoriatic Disease Activity Index (mCPDAI) were evaluated using Spearman correlation.

Results: The mean (SD) RAPID3 score at baseline was 16.9 (5.19). At wk24, patients in the GUS group (n=100) achieved statistically significantly greater decrease from baseline (improvement) in RAPID3 (-5.81 $\pm$ 6.0) than the PBO group (n=49) (-0.57 $\pm$ 5.1, $p<0.001$), and 50% of patients in the GUS group vs. 20.4% in the PBO group achieved an MID ($p<0.001$). Higher RAPID3 remission rate in the GUS than the PBO group (14.0% vs. 2.4%, $p=0.022$) was observed. The mean $\pm$ SD decrease from baseline in RAPID3 was -6.36 $\pm$ 6.2 at wk24, and -7.48 $\pm$ 6.3 at wk44 in those who continued Guselkumab (N=86). Among patients who switched from PBO to GUS at wk24 (N=28), mean $\pm$ SD change from baseline (improvement) in RAPID3 was -2.28 $\pm$ 5.2 at wk24 while on placebo and -7.60 $\pm$ 6.6 at wk44 after switching to GUS. The RAPID3 score was highly correlated with PASDAS ($r=0.84$, $p<0.001$), GRACE index ($r=0.89$, $p<0.001$), DAPSA ($r=0.77$ $p<0.001$) and mCPDAI ($r=0.65$, $p<0.001$) at wk16.

Conclusion: GUS-treated PsA patients demonstrated significant improvement in RAPID3 compared to PBO. RAPID3 is simple and feasible to use in routine clinical care, and it correlates well with other comprehensive PsA-specific disease activity measures.

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