POSTER perspectives

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Ixekizumab Exhibits a Favorable Safety Profile during 24 Weeks of Treatment in Subjects with Active Psoriatic Arthritis: Integrated Safety Analysis of Two Randomized, Placebo Controlled, Pase III Clinical Trials

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Background/Purpose: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets IL-17A. The objective of this analysis is to report the integrated safety of IXE in 2 pivotal trials in patients with active PsA.

Methods: The SPIRIT phase 3 trials consist of patients with active PsA who were bDMARD-naive (SPIRIT-P1, NCT01695239) or were inadequate responders to TNF-inhibitors (SPIRIT-P2; NCT02349295). Patients were randomized to 80 mg IXE every 4 weeks (Q4W, N=229) or 2 weeks (Q2W, N=225) after a 160 mg starting dose or PBO (N=224). Integrated safety data are presented from the PBO-controlled treatment periods (Weeks 0-24). Safety was assessed for patients who received at least 1 dose of study drug. At Week 16, patients deemed Inadequate Responders received rescue therapy and were included in this dataset only up to Week 16. Data was analyzed using a Cochran-Mantel-Haenszel test stratified by trial.

Results: The percentage of patients with ≥1 treatment emergent adverse event (TEAE) was significantly greater in the IXE compared to PBO treatment groups (Table 1). No clear difference was seen between groups for the percentage of patients with ≥1 serious adverse event (SAE) or discontinued early from study drug. Infection-related SAEs were reported in a significantly higher percentage of IXE Q2W than PBO patients. Treatment-emergent infections were numerically more frequent with IXE treatment compared to PBO (Table 2); upper respiratory tract infections, nasopharyngitis, and sinusitis were the most common infections. One PBO, 4 IXE Q4W, and 8 IXE Q2W-treated patients had ≥1 *Candida* infection. Injection site reactions were reported in a significantly higher percentage of patients in the IXE than the PBO treatment groups; most were of mild or moderate severity. Allergic reactions/hypersensitivity events were reported in a significantly higher percentage of IXE Q2W than PBO patients; no case of anaphylaxis was reported. Two cases of malignancy were reported (both IXE Q4W patients): prostate cancer and basal cell carcinoma. There were no major adverse cardiac events (MACE). While there were no reports of Crohn's disease or ulcerative colitis, 1 IXE Q2W patient had SAEs of anal abscess and anal fistula, considered to represent inflammatory bowel disease; this patient continued study drug. There were no deaths or reports of suicide or suicidal ideation.

Conclusion: The safety profile of IXE during the placebo-controlled treatment period was consistent with published findings in patients receiving ixekizumab for moderate-to-severe plaque psoriasis[1].

[1]Strober, B et al. *JAAD*. 2017; 76(3):432.

ABSTRACT NUMBER: 605

Event Type:	PBO (N=224)	IXE Q4W (N=229)	IXE Q2W (N=225)	Total IXE (N=454)
Patients with ≥1 TEAE	127 (57%)	153 (67%)*	156 (69%)*	309 (68%)*
Mild	60 (27%)	91 (40%)	81 (36%)	172 (38%)
Moderate	63 (28%)	54 (24%)	61 (27%)	115 (25%)
Severe	4 (2%)	8 (4%)	14 (6%)*	22 (5%)
Patients with ≥1 SAE	6 (3%)	9 (4%)	11 (5%)	20 (4%)
Infection-related SAE	0	1 (<1%)	5 (2%)*	6 (1%)
Discontinuation due to AE	8 (4%)	7 (3%)	12 (5%)	19 (4%)

Table 1. Overview of Adverse Events for the Integrated PBO-Controlled Treatment Period (Weeks 0-24).

Data depicted as n (%). Patients with multiple occurrences of the same event are categorized by the highest severity. *Statistically significant (p<.05) compared with placebo.

Event Type:	PBO (N=224)	IXE Q4W (N=229)	IXE Q2W (N=225)	Total IXE (N=454)
Infection	62 (28%)	77 (34%)	72 (32%)	149 (33%)
Candida	1 (<1%)	4 (2%)	8 (4%)*	12 (3%)
Cytopenias	2 (1%)	2 (1%)	4 (2%)	6 (1%)
Grade 3 or 4 Neutropenia	0	0	0	0
Injection-site reactions	10 (4%)	40 (17%)*	57 (25%)*	97 (21%)*
Allergic reactions/ hypersensitivities	4 (2%)	10 (4%)	14 (6%)*	24 (5%)*
Malignancies	0	2 (1%)	0	2 (<1%)
MACE	0	0	0	0
Depression	3 (1%)	4 (2%)	4 (2%)	8 (2%)
Interstitial Lung Disease	0	0	0	0
Hepatic Events	10 (4%)	7 (3%)	11 (5%)	18 (4%)
Crohn's Disease	0	0	0	0
Ulcerative Colitis	0	0	0	0

Table 2. Adverse Events of Special Interest for the Integrated PBO-Controlled Treatment Period (Weeks 0-24).

Data depicted as n (%). Reported as adverse events according to the high level term in MedDRA (Medical Dictionary for Regulatory Activities) *Statistically significant (p<.05) compared with placebo.

ABSTRACT NUMBER: 605

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