Ixekizumab Improves Nail and Skin Lesions in Patients With Active Psoriatic Arthritis and Prior TNF-Inhibitor Inadequate Response: 3-Year Results From SPIRIT-P2

P0383

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BACKGROUND

- Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with peripheral arthritis, enthesitis, dactylitis, spondyloarthritis, and psoriasis (PsO)[1,2]
- A significant correlation between fingernail PsO and PsA is established; nail PsO is persistent, slow to resolve, difficult to treat, and results in distinct impairment in daily activities[3]
- Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A[4]
- In SPIRIT-P2, ixekizumab has shown efficacy in patients with active PsA who had an inadequate response or intolerance to 1 or 2 tumor necrosis factor inhibitors (TNFi)[5]
  - In this population of patients, generally considered to be more difficult to treat and in whom reduced efficacy is often anticipated, ixekizumab provided significantly greater reduction, including clearance, of fingernail and skin lesions at 52 weeks compared to placebo[6]

OBJECTIVE

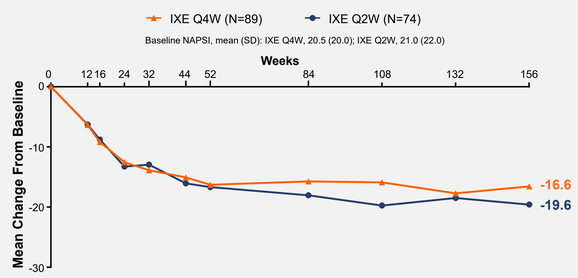
- To evaluate the efficacy of ixekizumab treatment over 3 years on nail and skin PsO in patients with active PsA with an inadequate response or intolerance to TNFi

ABBREVIATIONS

AE=adverse event; BSA=body surface area; CASPAR=Classification Criteria for Psoriatic Arthritis; cDMARD=conventional disease-modifying antirheumatic drug; IL=interleukin; IR=incidence rate; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; MedDRA=Medical Dictionary for Regulatory Activities; MTX=methotrexate; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index; PBO=placebo; PsA=psoriatic arthritis; PsO=psoriasis; PY=patient-years (total time patients were in the treatment period); R=randomization; RT=rescue therapy; SAE=serious adverse event; SD=standard deviation; sPGA=static Physician's Global Assessment; SJC=swollen joint count; TEAE=treatment-emergent adverse event; TJC=tender joint count; TNFi=tumor necrosis factor inhibitor

KEY RESULTS

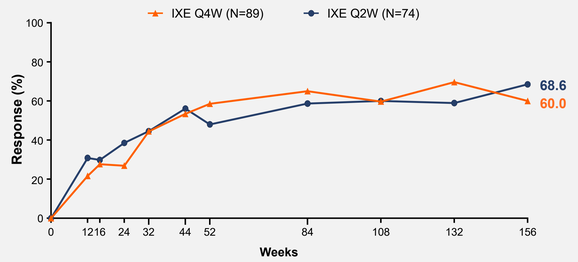
Mean Change From Baseline in NAPSI, Observed



Analyses conducted in patients with baseline fingernail involvement

- Decreases in mean Nail Psoriasis Severity Index (NAPSI) total score with ixekizumab treatment persisted through 3 years in patients with a prior inadequate response to TNFi

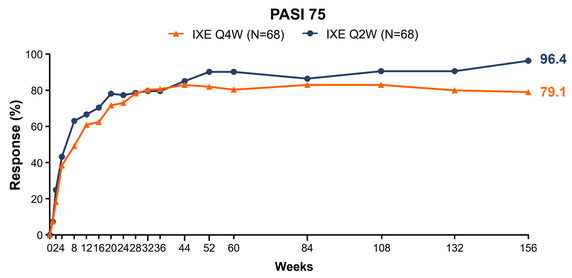
NAPSI (0) Response Rate, Observed

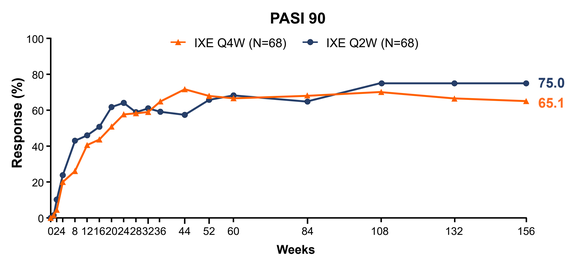


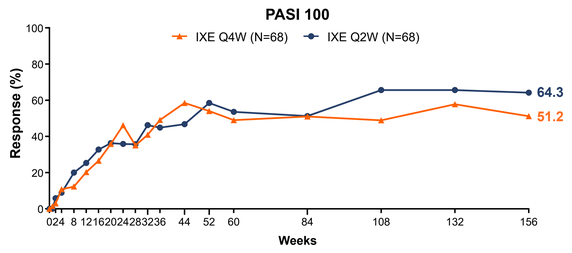
Analyses in patients originally randomized to ixekizumab with baseline fingernail involvement

- Increases in NAPSI (0) response rates with ixekizumab treatment persisted through 3 years in patients with a prior inadequate response to TNFi

PASI 75/90/100 Response Rates, Observed



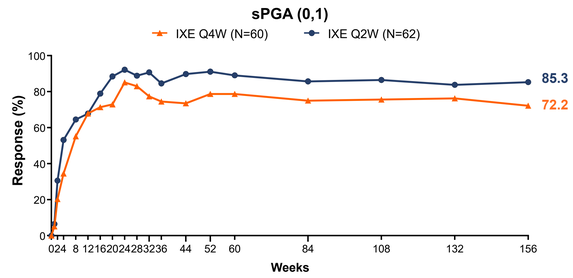


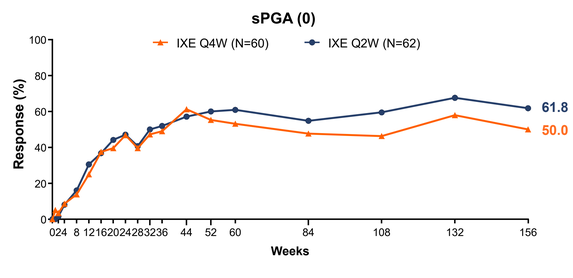


Baseline PASI with baseline psoriatic lesions ≥3% BSA, mean (SD): IXE Q4W, 9.3 (9.1); IXE Q2W, 8.8 (10.3)
Analyses conducted in patients originally randomized to ixekizumab with baseline psoriatic lesions ≥3% BSA

- Increases in Psoriasis Area and Severity Index 75/90/100 response rates with ixekizumab treatment persisted through 3 years in patients with a prior inadequate response to TNFi

sPGA (0,1) and (0) Response Rates, Observed





Analyses conducted in patients with baseline sPGA ≥3

- Increases in static Physician's Global Assessment (0,1) and (0) response rates with ixekizumab treatment persisted through 3 years in patients with a prior inadequate response to TNFi

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CONCLUSIONS

- In patients with active PsA and a prior inadequate response to TNFi, ixekizumab treatment resulted in persistent reduction and clearance of nail and skin lesions consistently over 3 years of treatment
- Results of these analyses are consistent with previous studies in patients with moderate-to-severe PsO, which have demonstrated the ability of ixekizumab treatment to clear nail and skin PsO[8]

DISCLOSURES

- **A. W. Armstrong** has been an investigator, advisor, and/or speaker for: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Regeneron, Sanofi, and Valeant Pharmaceuticals; **W. Tillet** has received grants, speaker fees, or honoraria from: AbbVie, Amgen, Celgene, Eli Lilly and Company, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, and UCB Pharma; **N. Somani**, **A. M. Gellett**, and **V. J. Geneus** are current employees and shareholders of: Eli Lilly and Company; **J. F. Merola** is a consultant and/or investigator for: AbbVie, Arena Pharmaceuticals, Avotres, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, EMD Serono, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB Pharma; **A. Tosti** is a consultant for: Almirall, Bristol Myers Squibb, DS Laboratories, Eli Lilly and Company, LEO Pharma, Monat Global, Procter & Gamble, and Thirty Madison; **A. Gottlieb** has received honoraria as an advisory board member and consultant for: Avotres, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, Janssen, LEO Pharma, Novartis, Sun Pharma, UCB Pharma, and XBiotech (stock options); and has received research/educational grants for her institution from: Boehringer Ingelheim, Janssen, Novartis, Sun Pharma, UCB Pharma, and XBiotech; **P. A. Rich** has received grant/research support from: AbbVie, Allergan, Anacor Pharmaceuticals, Boehringer Ingelheim, Cassiopea, Cellceutix, Cutanea, Dermira, Eli Lilly and Company, Galderma Laboratories, Janssen Ortho, Kadmon, LEO Pharma, Merck, Moberg Derma, Novartis, Pfizer, Ranbaxy Laboratories, Sandoz, and Viamet
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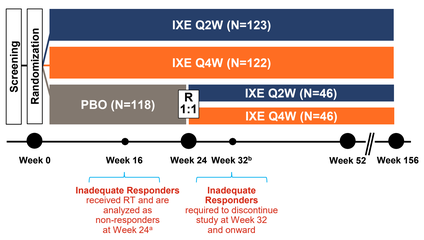
METHODS

SPIRIT-P2 (TNFi-Experienced) Study Design[5,7]

Double-blind Treatment and Extension Periods



[a] All inadequate responders (as determined by prespecified, blinded TJC and SJC criteria) at Week 16 received RT and were analyzed as non-responders after Week 16; PBO inadequate responders received their first dose of ixekizumab at Week 16. [b] Patients were discontinued from the study if they did not meet the defined response criteria at Week 32 (≥20% improvement from baseline in TJC and SJC) and any subsequent visit during the study

Key Eligibility Criteria

Inclusion

- ≥18 years of age
- Established active PsA ≥6 months and currently meet CASPAR:
  - ≥3 tender joints and ≥3 swollen joints
- Prior treatment with ≥1 cDMARD[a] and 1-2 TNFi (TNFi discontinued owing to inadequate response or intolerance)
- Active psoriatic skin lesion or documented personal history of PsO

Exclusion

- Current or recent use[b] of ≥1 biologic agent for the treatment of PsA or PsO
- Current use of >1 cDMARD[a] at study entry
- Previous treatment with α4-integrin–, IL-17–, or IL-12/23–targeted monoclonal antibodies
- Diagnosis of active inflammatory arthritis syndromes or spondyloarthropathies other than PsA
- Serious infection ≤3 months

[a] MTX, sulfasalazine, leflunomide, or hydroxychloroquine; [b] Etanercept <28 days; infliximab, adalimumab, certolizumab pegol, or alefacept <60 days; golimumab <90 days; rituximab <12 months; or any other biologic agent or small molecule <5 half-lives prior to baseline

Efficacy Measures

PASI
- PASI 75/90/100 responses
  - In patients with ≥3% BSA involvement

sPGA
- sPGA (0,1) and sPGA (0) responses
  - In patients with baseline sPGA ≥3

NAPSI
- NAPSI (0) response (resolution of symptoms)
- NAPSI change from baseline
  - In patients with baseline fingernail involvement

Statistical Analysis

- Efficacy for the Intent-to-Treat population randomized at Week 0 to ixekizumab was assessed through Week 156
  - Mean change from baseline and response rate were reported as observed
  - Patients randomized to placebo were excluded from the analyses
- Safety analyses were performed on the total population of patients who received ≥1 dose of ixekizumab at any time from Week 0 to 156, including patients randomized to placebo at Week 0 who were subsequently randomized to ixekizumab at Week 16 (inadequate responders) or Week 24

RESULTS

Baseline Demographics and Clinical Characteristics

	IXE Q4W (N=122)	IXE Q2W (N=123)
Age, years	52.6 (13.6)	51.7 (11.9)
Male, n (%)	63 (51.6)	50 (40.7)
Time since PsA diagnosis, years	11.0 (9.6)	9.9 (7.4)
TJC (68 joints)	22.0 (14.1)	25.0 (17.3)
SJC (66 joints)	13.1 (11.2)	13.5 (11.5)
Patients with PsO, n (%)	118 (96.7)	113 (91.9)
Time since PsO diagnosis, years	15.7 (12.3)	16.5 (13.0)
NAPSI score[a]	20.5 (20.0)	21.0 (22.0)
% BSA in patients with baseline PsO	12.5 (17.4)	11.6 (18.6)
Background cDMARD therapy		
Current use, n (%)	60 (49.2)	73 (59.3)
MTX, n (%)	48 (39.3)	61 (49.6)
MTX mean weekly dose, mg	15.9 (4.8)	16.0 (4.6)
Previous TNFi therapy, n (%)		
Inadequate response to 1 TNFi	71 (58.2)	65 (52.8)
Inadequate response to 2 TNFi	41 (33.6)	46 (37.4)
Intolerant to a TNFi	10 (8.2)	12 (9.8)

Data are mean (SD) unless stated otherwise
Data from Intent-to-Treat population who were initially randomized to IXE Q4W or IXE Q2W at Week 0
[a] In patients with baseline fingernail involvement; IXE Q4W n=88, IXE Q2W n=73

Safety Overview, AEs, Weeks 0-156

n (IR)[a]	IXE Q4W (N=168; PY=345.1)	IXE Q2W (N=169; PY=298.9)
TEAEs	141 (40.9)	145 (48.5)
Mild	41 (11.9)	43 (14.4)
Moderate	85 (24.6)	74 (24.8)
Severe	15 (4.3)	28 (9.4)
SAEs	19 (5.5)	23 (7.7)
Discontinuations due to AEs[b]	17 (4.9)	21 (7.0)
Death[b]	1 (0.3)	2 (0.7)
Infections	112 (32.5)	101 (33.8)
Serious infections	5 (1.4)	5 (1.7)
Injection-site reactions	25 (7.2)	42 (14.1)
Discontinuation due to injection-site reactions	1 (0.3)	1 (0.3)
Inflammatory bowel disease[c]	1 (0.3)	1 (0.3)
Reported by investigator	1 (0.3)	1 (0.3)
Confirmed by adjudication	0	0

[a] Patients may have multiple events per category; [b] Deaths are also included as SAEs and study treatment discontinuations owing to AEs; [c] Inflammatory bowel disease was identified by MedDRA terms based on investigator; cases were reviewed by an independent committee of experts for adjudication

- The 3-year safety profile of ixekizumab-treated patients in SPIRIT-P2 was consistent with that previously observed in patients with active PsA and patients with moderate-to-severe PsO who received ixekizumab

Study was sponsored by Eli Lilly and Company