Efficacy, Health-Related Outcomes, and Safety of Ixekizumab for Up to Five Years of Open-Label Treatment in a Phase 2 Study in Chronic Plaque Psoriasis

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BACKGROUND

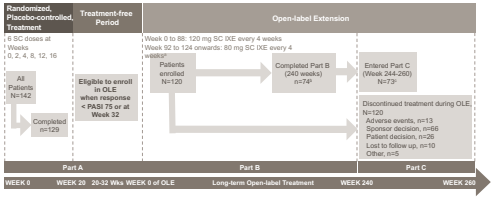
- Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A[1]
  - Demonstrated significant efficacy in the treatment of moderate-to-severe psoriasis[2-5]
  - Maintained improvements in skin clearance for up to 4 years in an open-label extension of a Phase 2 trial[6]

OBJECTIVE

- To assess the efficacy, health-related outcomes, and safety of ixekizumab after 5 years of treatment in the open-label extension of a Phase 2 trial (NCT01107457)

METHODS

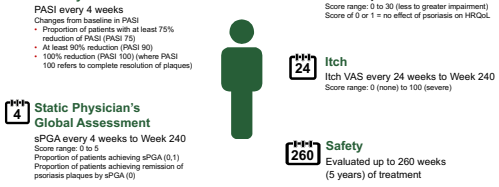
Figure 1. Study Design



[a] The IXE dose was reduced to 80 mg following a protocol amendment to align with the dose regimen used in Phase 3 trials
[b] Includes ongoing patients
[c] Patient consent was required to continue beyond Week 240
IXE=ixekizumab; OLE=open-label extension; PASI 75=Psoriasis Area and Severity Index 75% response; SC=subcutaneous; sPGA=static Physician's Global Assessment

- Study included patients with chronic plaque psoriasis for ≥6 months, ≥10% body surface area involvement, static Physician's Global Assessment ≥3, and Psoriasis Area and Severity Index ≥12

Figure 2. Assessments



DLQI=Dermatology Life Quality Index; HRQoL=Health-related quality of life; PASI=Psoriasis Area and Severity Index; sPGA=static Physician's Global Assessment; VAS=Visual Analog Scale

Statistical Analyses

- Descriptive statistics (N, mean change, 95% confidence intervals) are provided
- Any imputation was performed using the last observation carried forward method

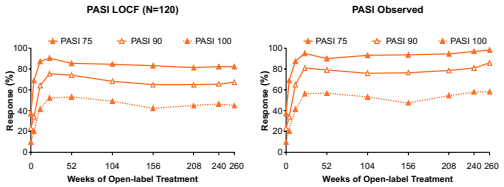
RESULTS

Table 1. Baseline Demographics and Disease Characteristics at the Start of Part B (Open-label Extension)

Characteristic	N=120
Age, years	47.2 (12.3)
Male, n (%)	70 (58.3)
Body weight, kg	95.4 (26.4)
PASI	17.9 (5.9)
Nail psoriasis, n (%)	52 (43.3)
NAPSI	40.5 (41.7)
Scalp psoriasis, n (%)	91 (75.8)
PSSI	19.3 (13.3)
DLQI	10.9 (6.1)
Itch VAS	58.3 (26.0)
PatGA (0,1) n (%)	1 (0.8)

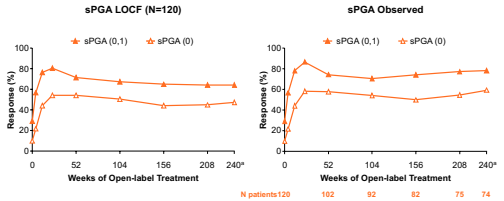
Values are mean (standard deviation) unless otherwise stated
DLQI=Dermatology Life Quality Index; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index; PatGA=Patient's Global Assessment of Disease Activity; PSSI=Psoriasis Scalp Severity Index; VAS=Visual Analog Scale

Figure 3. PASI Response Rates With Ixekizumab Were Maintained Over 5 Years of Open-label Treatment



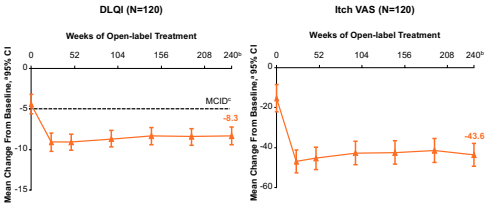
Data points shown at Weeks 0, 4, 12, 24, 52, 104, 156, 208, 240, 260
LOCF=last observation carried forward; PASI 75/90/100=Psoriasis Area and Severity Index 75%/90%/100% response

Figure 4. sPGA Response Rates With Ixekizumab Were Maintained Over 4.5 Years of Open-label Treatment



Data points shown at Weeks 0, 4, 12, 24, 52, 104, 156, 208, 240
[a] sPGA was only collected to Week 240, per protocol
LOCF=last observation carried forward; sPGA=static Physician's Global Assessment

Figure 5. Ixekizumab Provides Sustained Improvements in DLQI and Itch Reduction in Moderate-to-Severe Psoriasis Through 4.5 Years of Treatment, LOCF



Data points shown at Weeks 0, 24, 48, 96, 144, 192, 240
[a] Defined as the last available value before the first dose in the randomized, placebo-controlled treatment period
[b] DLQI and Itch VAS were only collected to Week 240, per protocol
[c] MCID for DLQI is improvement from baseline ≥5[7]
CI=confidence interval; DLQI=Dermatology Life Quality Index; LOCF=last observation carried forward; MCID=minimal clinically important difference; VAS=Visual Analog Scale

Table 2. Incidence of Treatment-emergent Adverse Events Over Time

	Adverse Events, n (%)					
	≥1 to ≤52 Weeks (N=120, PY=108)	>52 to ≤104 Weeks (N=102, PY=95)	>104 to ≤156 Weeks (N=90, PY=86)	>156 to ≤208 Weeks (N=83, PY=80)	>208 to ≤260 Weeks (N=76, PY=72)	≥1 Day (N=120, PY=455)
TEAEs	72 (60.0)	68 (66.7)	65 (72.2)	54 (65.1)	38 (50.0)	105 (87.5)
SAEs	7 (5.8)	4 (3.9)	6 (6.7)	4 (4.8)	8 (10.5)	24 (20.0)

PY=person years; SAE=serious adverse event; TEAE=treatment-emergent adverse event

- Throughout the open-label extension, most treatment-emergent adverse events were considered mild or moderate overall
- Among the 24 patients experiencing ≥1 treatment-emergent serious adverse event, the most frequent (>4%) were: infections and infestations (n=6, 5.0%), cardiac disorders (n=5, 4.2%) and benign, malignant and unspecified neoplasms (n=5, 4.2%)

Table 3. Most Common (≥10%) Adverse Events During Open-label Treatment

System Organ Class Preferred Term	Incidence, n (%) (N=120)
Infections and infestations	83 (69.2)
Nasopharyngitis	29 (24.2)
Sinusitis	17 (14.2)
Upper respiratory tract infection	15 (12.5)
Urinary tract infection	13 (10.8)
Nervous system disorders	22 (18.3)
Headache	12 (10.0)

Table 4. Adverse Events Leading to Discontinuation During Open-label Treatment

	Incidence, n (%) (N=120)
Discontinued due to an adverse event	13 (10.8)
Exposure during pregnancy	2 (1.7)
Alanine aminotransferase increased	1 (0.8)
Hepatic enzyme increased	1 (0.8)
Hidradenitis	1 (0.8)
Invasive ductal breast carcinoma	1 (0.8)
Non-small cell lung cancer metastatic	1 (0.8)
Osteomyelitis	1 (0.8)
Psoriatic arthropathy	1 (0.8)
Pyelonephritis	1 (0.8)
Rectal adenocarcinoma	1 (0.8)
Rectal adenoma	1 (0.8)
Urinary tract obstruction	1 (0.8)

CONCLUSIONS

- Ixekizumab provided sustained complete to near complete skin clearance up to 5 years
  - PASI 75 at Week 260: 83% (LOCF)/98% (observed)
  - PASI 90 at Week 260: 68% (LOCF)/86% (observed)
  - PASI 100 at Week 260: 45% (LOCF)/58% (observed)
  - sPGA (0,1) at Week 240: 64% (LOCF)/78% (observed)
  - sPGA (0) at Week 240: 48% (LOCF)/59% (observed)
- Ixekizumab provided sustained improvements in DLQI and Itch reduction through 4.5 years of treatment
  - DLQI mean change from baseline at Week 240: -8.3 (LOCF)
  - Itch VAS mean change from baseline at Week 240: -43.6 (LOCF)
- The most common adverse events occurring during the open-label treatment period were consistent with those previously reported in clinical results for patients treated with ixekizumab for a shorter time period[1-4]

DLQI=Dermatology Life Quality Index; LOCF=last observation carried forward; PASI 75/90/100=Psoriasis Area and Severity Index 75%/90%/100% response; sPGA=static Physician's Global Assessment; VAS=Visual Analog Scale

Disclosures

- **A. Blauvelt** has served as a scientific adviser and/or clinical study investigator for: AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Genentech/Roche, GlaxoSmithKline, Janssen, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB, Valeant, and Vidac, and as a paid speaker for Eli Lilly and Company, Janssen, Regeneron, and Sanofi Genzyme; **K. Gordon** has served as a consultant for: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly and Company, Janssen, Novartis, and Pfizer, and has received grants from: AbbVie, Amgen, Celgene, Eli Lilly and Company and Janssen; **C. Leonardi** is on the speaker's bureau of: AbbVie, Celgene, and Leo Pharma, is a consultant for: AbbVie, Amgen, Dermira, Eli Lilly and Company, Janssen, Leo Pharma, Pfizer, Sandoz, and UCB Pharma, has a conflict with: Actavis, AbbVie, Amgen, Celgene, Cohenus, Cermira, Eli Lilly and Company, Galderma, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Sandoz, Stiefel, and Wyeth; **C. Zachariae** has received honoraria from: Eli Lilly and Company, Novartis, and Pfizer, and has consulted for and participated in advisory boards for: AbbVie, Amgen, Eli Lilly and Company, Janssen-Cilag, Novartis, and Takeda and has been a clinical study investigator for: AbbVie, Amgen, Eli Lilly and Company, Leo Pharma, MSD, Novartis, Regeneron, and Takeda; **R. Burge**, **T. Ridenour**, **M. McKean-Matthews**, **S. Garces**, and **G. Cameron** are shareholders and employees of Eli Lilly and Company
- This study was sponsored by Eli Lilly and Company. Medical writing services were provided by Samantha Forster, PhD, of ProScribe – part of the Envision Pharma Group, and were funded by Eli Lilly and Company

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2017 Fall Clinical Dermatology Conference (Fall CDC 2017); Las Vegas, Nevada; October 12-15, 2017; Previously presented at EADV 2017

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