Efficacy and Safety of Ixekizumab in a Randomized, Double-Blinded, Placebo-Controlled, Phase 3b Clinical Trial in Patients With Moderate-to-Severe Genital Psoriasis

Caitríona Ryan,[1] Alan Menter,[2] Lyn Guenther,[3] Andrew Blauvelt,[4] Robert Bissonnette,[5] Fan Emily Yang,[6] Alison Potts Bleakman,[6] David A Amato[6]

[1]Department of Dermatology St Vincent's Hospital, Dublin, Ireland; [2]Menter Cosmetic Institute, Dallas, TX, USA; [3]Guenther Research Inc., London, Canada; [4]Oregon Medical Research Center, Portland, OR, USA; [5]Innovaderm Research, Montreal, Canada; [6]Eli Lilly and Company, Indianapolis, IN, USA

SYNOPSIS

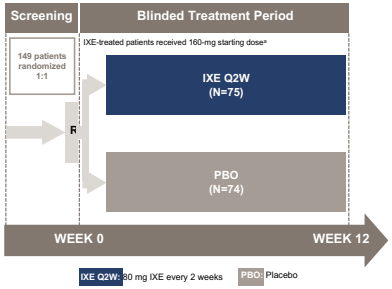
- Genital psoriasis is common (up to 60%) in patients with plaque psoriasis[1]
- Can have a significant impact on quality of life and sexual health[1,2]
- Limited data exist from clinical trials on the efficacy of treatments for genital psoriasis
- Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A[3] and is approved for the treatment of plaque psoriasis

OBJECTIVE

- To evaluate the effect of ixekizumab on the severity of genital psoriasis compared with placebo during 12 weeks of treatment

STUDY DESIGN

IXORA-Q



[a]Given as 2 subcutaneous injections of 80 mg IXE at Week 0. Patients assigned to placebo received 2 subcutaneous injections of placebo at Week 0
IXE=ixekizumab; R=randomization

Key Eligibility Criteria

Inclusion Criteria

- Male or female ≥18-years-old
- Chronic plaque psoriasis for ≥6 months
- Plaque psoriasis in a non-genital area
- static Physician's Global Assessment (sPGA) of genitalia ≥3
- Overall sPGA ≥3
- Body surface area (BSA) ≥1%[a]
- Failed to respond to/intolerant of ≥1 topical therapy[b] for genital psoriasis

Exlusion Critera

- Recent suicide attempt (≤30 days), suicide risk, or Quick Inventory of Depressive Symptomatology–Self Report (QIDS-SR[16]) Item 12 score of 3
- Significant uncontrolled cardiovascular, cerebrocardiovascular, or other unstable medical or psychiatric conditions
- Active or recent infection that would pose an unacceptable risk to the patient
- Received/currently receiving treatment for active candidiasis or tinea in the genital area
- Received treatment with interleukin-17 (IL-17) antagonists

[a]Approximately 40% of patients enrolled were to have had BSA involvement of 1% to <10%, and the majority were to have had ≥10% BSA involvement
[b]Corticosteroids, calcineurin inhibitors, and/or vitamin D analogs

Primary Endpoint

- Proportion of patients achieving sPGA of genitalia (0,1)

sPGA of Genitalia

- Measurement of the patient's psoriasis severity in the genital region at a given time point on a 6-point scale:

Major Secondary Endpoints

- Proportion of patients achieving overall static physician global assessment [sPGA (0,1)]
- Proportion of patients achieving a ≥3-point improvement in genital itch numeric rating scale (gen-itch NRS)
  - Among patients with a baseline score of ≥3
- Proportion of patients whose frequency of sexual activity was never or rarely limited by genital psoriasis [Sexual Frequency Questionnaire (SFQ) Item 2 score 0 or 1]
  - Among patients with a baseline score ≥2

SFQ Item 2	In the past week, how often did your genital psoriasis limit the frequency of your sexual activity?	Never	0
		Rarely	1
		Sometimes	2
		Often	3
		Always	4

Statistical Analysis

- **Efficacy:** Intent-to-Treat Population
  - All patients who were randomized
- **Safety**: Safety Population
  - Randomized patients who received at least one dose
- **Efficacy outcomes:** Evaluated using a logistic regression model
  - Factors: treatment and BSA involvement (<10% or ≥10%)
  - Missing values imputed by non-responder imputation
  - Secondary analysis was conducted using a Fisher's exact test

BSA=body surface area

RESULTS

Baseline Demographics and Disease Characteristics

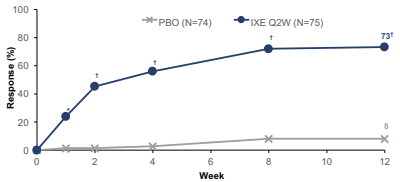
	PBO (N=74)	IXE Q2W (N=75)
Age, years	44.4 (12.6)	43.1 (13.0)
Male, n (%)	57 (77)	56 (75)
Weight, kg	95.1 (26.3)	91.9 (23.1)
Time since psoriasis onset, years	16.1 (12.5)	16.9 (12.8)
Time since genital psoriasis onset, years	8.3 (8.2)	9.3 (10.0)
Percentage of BSA involved	16.8 (15.7)	14.2 (12.6)
BSA 1 to <10%, n (%)	28 (38)	31 (41)
BSA ≥10%, n (%)	46 (62)	44 (59)
sPGA of genitalia	3.5 (0.5)	3.4 (0.6)
sPGA of genitalia=3, n (%)	41 (55)	45 (61)
sPGA of genitalia=4, n (%)	32 (43)	27 (36)
sPGA of genitalia=5, n (%)	1 (1.4)	2 (2.7)
sPGA overall	3.5 (0.6)	3.5 (0.6)

Data are mean (standard deviation) unless otherwise stated
BSA=body surface area; IXE Q2W=80 mg ixekizumab every 2 weeks; PBO=placebo; sPGA=static Physician's Global Assessment

sPGA of Genitalia (0,1) Response Rate

NRI, Blinded Treatment Period, ITT Population

- 7 out of 10 ixekizumab-treated patients achieved clear or almost clear genital skin at Week 12
- Percentage of patients achieving clear or almost clear genital skin was significantly greater for ixekizumab as early as Week 1

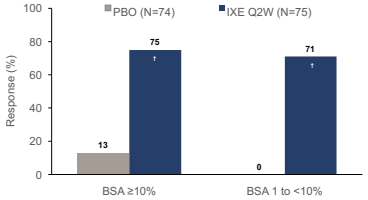


*p<.01 vs. PBO; † p<.001 vs. PBO
ITT=intent-to-treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician's Global Assessment

sPGA of Genitalia (0,1) Response Rate by BSA

NRI, Blinded Treatment Period, ITT Population

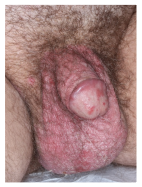
- The sPGA of genitalia (0,1) response with ixekizumab at Week 12 was consistent, regardless of the percent BSA involved at baseline



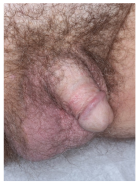
†p<.001 vs. PBO
BSA=body surface area; ITT=intent-to-treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician's Global Assessment

Photos: Male Patient Treated With Ixekizumab

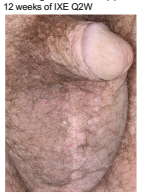
Week 0
sPGA of genitalia = severe (4)
Randomized to IXE Q2W



Week 2
sPGA of genitalia = minimal (1)
2 weeks of IXE Q2W



Week 12
sPGA of genitalia = clear (0)
12 weeks of IXE Q2W

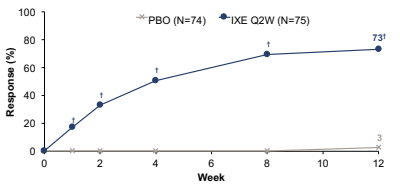


IXE Q2W=80 mg ixekizumab every 2 weeks; sPGA=static Physician's Global Assessment

Overall Skin sPGA (0,1) Response Rate

NRI, Blinded Treatment Period, ITT Population

- 7 out of 10 ixekizumab-treated patients achieved clear or almost clear skin overall at Week 12
- Percentage of patients achieving clear or almost clear skin overall was significantly greater for ixekizumab as early as Week 1

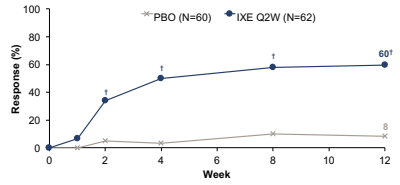


†p<.001 vs. PBO
ITT=intent-to-treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; sPGA=static Physician's Global Assessment

Gen-Itch NRS Response[a] Rate

NRI, Blinded Treatment Period, ITT Population With Baseline Gen-Itch NRS ≥3

- 6 out of 10 ixekizumab-treated patients had clinically meaningful improvements[a] in genital itch at Week 12
- Percentage of patients achieving clinically meaningful improvement in genital itch was significantly greater for ixekizumab as early as Week 2

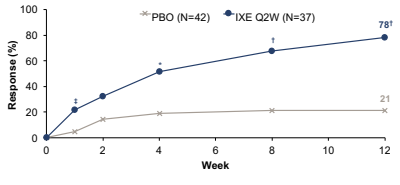


†p<.001 vs. PBO
[a]≥3 point improvement in gen-itch NRS
gen-itch NRS=genital itch numeric rating scale; ITT=intent-to-treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo

SFQ Item 2 Score (0,1) Response Rate

NRI, Blinded Treatment Period, ITT Population With Baseline SFQ Item 2 Score ≥2

- Approximately 8 out of 10 ixekizumab-treated patients were no longer or rarely limited by the impact of genital psoriasis on frequency of sexual activity at Week 12
- Percentage of patients who were no longer or rarely limited by the impact of genital psoriasis on frequency of sexual activity was significantly greater for ixekizumab as early as Week 1



‡p<.05 vs. PBO; *p<.01 vs. PBO; †p<.001 vs. PBO
ITT=intent-to-treat; IXE Q2W=80 mg ixekizumab every 2 weeks; NRI=non-responder imputation; PBO=placebo; SFQ=Sexual Frequency Questionnaire

Safety Overview

Blinded Treatment Period, Safety Population

	PBO (N=74)	IXE Q2W (N=75)
Overall TEAEs	33 (44.6)	42 (56.0)
Mild	15 (20.3)	23 (30.7)
Moderate	15 (20.3)	18 (24.0)
Severe	3 (4.1)	1 (1.3)
Serious adverse event	1 (1.4)[a]	0
TEAE related to study treatment	7 (9.5)	14 (18.7)
Discontinuation due to AEs	5 (6.8)[b]	1 (1.3)[c]
Most common TEAEs[d]		
Upper respiratory tract infection	5 (6.8)	11 (14.7)
Injection-site reactions	2 (2.7)	8 (10.7)
Headache	4 (5.4)	3 (4.0)
Oropharyngeal pain	2 (2.7)	3 (4.0)
Pruritus	2 (2.7)	3 (4.0)

Data represents n (%)
[a]Pancreatitis acute (n=1); [b] Worsening psoriasis (n=4), worsening psoriatic arthritis (n=1), liver function test increased (n=1); [c] Eczema (n=1); [d] Experienced by ≥4% of patients in the IXE Q2W arm
AE=adverse event; IXE Q2W=80 mg ixekizumab every 2 weeks; PBO=placebo; TEAE=treatment-emergent adverse event

CONCLUSIONS

- Ixekizumab was superior to placebo for the primary and all major secondary endpoints at Week 12, and significant improvements versus placebo were observed as early as Week 1
- Safety outcomes were consistent with the overall safety profile of ixekizumab[4-7]
- Ixekizumab:
  - Is an efficacious treatment for moderate-to-severe genital psoriasis, providing rapid clearance of genital skin
  - Improves genital itch
  - Minimizes how often genital psoriasis limits the frequency of sexual activity

Disclosures

- **D. Amato** is a full-time employee of Eli Lilly and Company and has stocks
- This study was sponsored by Eli Lilly and Company. Medical writing services were provided by Luke Carey, PhD, of ProScribe – part of the Envision Pharma Group, and were funded by Eli Lilly and Company

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Winter Clinical Dermatology Conference – 2018, Kaanapali, HI, USA; January 12-17, 2018; Previously presented at EULAR 2017

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