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Nail Psoriasis Does Not Affect Skin Response to Ixekizumab in Patients With Moderate-To-Severe Psoriasis

Phoebe Rich MD,[a] Orin Goldblum MD,[b] Damon Disch PhD,[b] Chen-Yen Lin PhD,[b] Joseph F. Merola MD,[c] Boni Elewski MD[d]

[a]Oregon Health and Science University's Center for Health and Healing, Portland, OR
[b]Eli Lilly and Company, Indianapolis, IN
[c]Brigham and Women's Hospital, Harvard Medical School, Boston, MA
[d]University of Alabama at Birmingham, Birmingham, AL

ABSTRACT

Background: Presence of nail psoriasis in patients with plaque psoriasis may be an indicator of greater disease severity. Previously, patients with nail psoriasis have had delayed skin clearance after treatment compared to patients without nail psoriasis.

Objective: This post-hoc analysis evaluated the efficacy of ixekizumab in clearance of plaque psoriasis in patients with and without nail psoriasis.

Methods: Data were integrated from two phase 3 clinical trials (UNCOVER-2 and UNCOVER-3; N=2570) to assess skin response over 12 weeks of treatment with subcutaneous placebo, etanercept, or ixekizumab in patients with and without nail psoriasis. Nail response was assessed using Nail Psoriasis Severity Index (NAPSI) and skin response was assessed as the percentage of patients achieving 75%, 90%, or 100% improvement in Psoriasis Area and Severity Index (PASI 75, PASI 90, PASI 100) or a score of 0 or 1 on the static Physician Global Assessment (sPGA 0 or 0,1).

Results: From baseline to week 12, progressive improvement in psoriasis occurred with ixekizumab and etanercept treatment; however, significantly more patients with nail psoriasis than without achieved PASI 75 at weeks 8 and 12 and sPGA (0,1) at week 12 with ixekizumab. Significantly more patients with severe nail psoriasis than mild achieved PASI 75 at weeks 8 and 12 with ixekizumab.

Conclusion: Patients with and without nail psoriasis responded well to ixekizumab. The presence of nail psoriasis did not negatively affect skin clearance in patients treated with ixekizumab.

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INTRODUCTION

Psoriasis is a chronic, inflammatory disease that affects millions of people in North America and Europe and is characterized by plaques that may appear on various parts of the body.[1] While skin manifestations are the most common characteristic of the disease, nail involvement is an often-overlooked clinical symptom. The prevalence of nail psoriasis is greater than 50% in patients with plaque psoriasis.[2]

Nail involvement may have a negative impact on patient's quality of life in addition to skin manifestations alone, and the management of nail psoriasis can be challenging.[3,4] The presence of nail psoriasis may be an indicator of disease chronicity or severity, as well as a strong indicator of psoriatic arthritis.[4,5] Many patients with nail psoriasis have reported pain as well as interference with daily activities and work productivity.[6] Nail psoriasis is widely acknowledged to be more difficult to treat than skin lesions.[7] Although there have been many recent advances in the treatment of skin psoriasis, the options for nail psoriasis are more limited. Additionally, previous studies have shown that patients with nail psoriasis treated with biological agents had delayed skin clearance compared to those without nail psoriasis.[8,9]

Ixekizumab, a humanized immunoglobulin G subclass 4 (IgG4), high-affinity, anti-interleukin (IL)-17A monoclonal antibody, has been shown in phase 2 and phase 3 clinical trials, including UNCOVER-2 and UNCOVER-3, to be effective in the clearance of plaque and nail psoriasis.[10-14] This post-hoc, integrated analysis of the UNCOVER-2 and UNCOVER-3 trials evaluates the effects of ixekizumab on plaque psoriasis in patients with varying levels of baseline nail involvement after 12 weeks of treatment.

MATERIALS AND METHODS

Study Design, Population, and Treatments

Data were integrated from the 12-week induction periods of two multicenter, randomized, double-blind, placebo-controlled phase 3 clinical trials (UNCOVER-2, NCT01597245; UNCOVER-3, NCT01646177). Individual trial designs were previously published.[10,11]

Eligible patients were ≥18 years of age with a confirmed diagnosis of moderate-to-severe plaque psoriasis.[11] Briefly, from week 0–12, patients were randomized to receive either subcutaneous placebo (PBO), etanercept 50 mg twice weekly (ETN), or ixekizumab 80 mg every 2 weeks (IXEQ2W) or every 4 weeks (IXEQ4W) after a 160-mg starting dose at week 0.

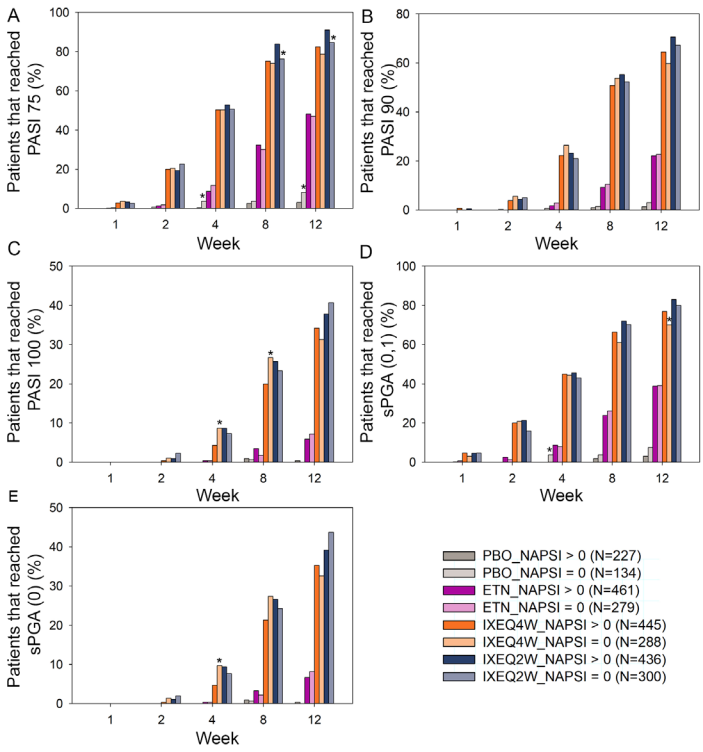
Study protocols were approved by the Institutional Review Board at each study center, and studies were conducted in accordance with the ethical principles of the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, the ICH GCP Guideline [E6], and applicable laws and regulations. Written informed consent was obtained from each patient at study entry before any study procedures occurred.

Efficacy Outcomes

Co-primary efficacy endpoints were the proportions of patients achieving Psoriasis Area and Severity Index (PASI) 75 or higher and static Physician Global Assessment (sPGA) (0,1) with at least a 2-point reduction from baseline at week 12.[10,11] Secondary efficacy endpoints at week 12 included proportions of patients achieving PASI 90, PASI 100, and sPGA (0; remission), and change from baseline in Nail Psoriasis Severity Index (NAPSI) score in patients with baseline fingernail involvement.

Patients were assessed at baseline for fingernail psoriasis using NAPSI. Each fingernail was divided with imaginary horizontal and longitudinal lines into quadrants scored for bed (score of 0–4) and matrix (score of 0–4) psoriasis depending on the presence (score of 1) or absence (score of 0) of any of the features of fingernail bed and fingernail matrix psoriasis in each quadrant. The NAPSI score of a fingernail is the sum of scores in fingernail bed and fingernail matrix from each quadrant (maximum of 8); then scores of all fingernails were added to obtain total NAPSI scores, ranging from 0 to 80 (no nail psoriasis to severe nail psoriasis, respectively). For the present analysis, patients were categorized by presence or absence of and severity of nail psoriasis as patients with nail psoriasis (NAPSI score >0 at baseline), patients without nail psoriasis (NAPSI=0 at baseline), patients with severe nail psoriasis (NASPI ≥16 at baseline), and patients with mild nail psoriasis (NAPSI <16 at baseline).

FIGURE 1. Proportion of patients achieving (A) PASI 75 (B) PASI 90 (C) PASI 100 (D) sPGA (0,1) or (E) sPGA (0) response through week 12 in patients with (NAPSI >0) and without (NAPSI=0) nail psoriasis.

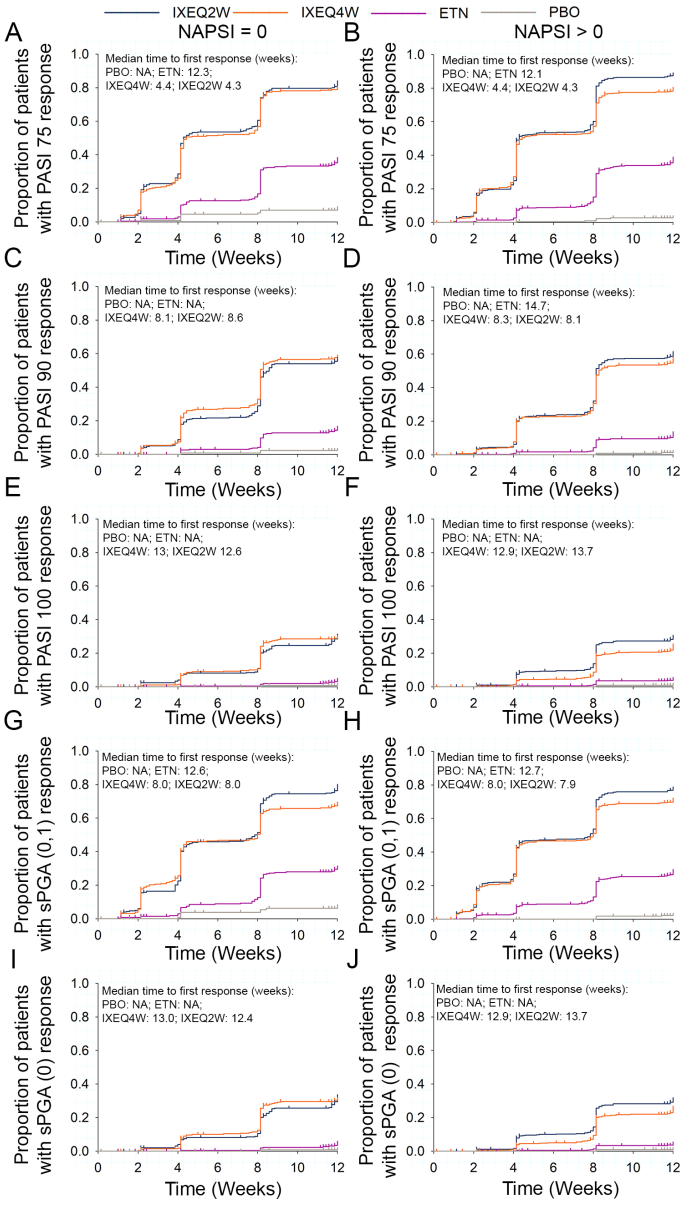


(A) Significantly more ($P<0.05$) patients treated with IXEQ4W and IXEQ2W with and without nail psoriasis reached PASI 75 from week 1 through 12 compared to ETN. Significantly more patients treated with IXEQ4W with and without nail psoriasis and IXEQ2W with nail psoriasis reached PASI 75 from week 1 through 12 compared to PBO. Significantly more patients treated with IXEQ2W without nail psoriasis reached PASI 75 from week 2 through 12 compared to PBO. Significantly more patients treated with ETN with and without nail psoriasis reached PASI 75 from week 4 through 12 compared with PBO. (B) Significantly more patients treated with IXEQ4W and IXEQ2W with and without nail psoriasis reached PASI 90 from week 2 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with nail psoriasis reached PASI 90 at week 4 compared with PBO. Significantly more patients treated with ETN with and without nail psoriasis reached PASI 90 from week 8 through 12 compared with PBO. (C) Significantly more patients treated with IXEQ2W with and without nail psoriasis reached PASI 100 compared to ETN at week 2. Significantly more patients treated with IXEQ2W and IXEQ4W with and without nail psoriasis reached PASI 100 from week 4 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with nail psoriasis reached PASI 100 at week 8 compared with PBO. Significantly more patients treated with ETN with and without nail psoriasis reached PASI 100 at week 12 compared with PBO. (D) Significantly more patients treated with IXEQ4W and IXEQ2W with and without nail psoriasis reached sPGA (0,1) from week 1 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with nail psoriasis reached sPGA (0,1) at week 2 through 4 compared with PBO. Significantly more patients treated with ETN with and without nail psoriasis reached sPGA (0,1) from week 8 through 12 compared with PBO. (E) Significantly more patients treated with IXEQ2W with and without nail psoriasis and IXEQ4W without nail psoriasis reached sPGA (0) compared to ETN at week 2. Significantly more patients treated with IXEQ4W and IXEQ2W with and without nail psoriasis reached sPGA (0) from week 4 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with and without nail psoriasis reached sPGA (0) at week 12 compared with PBO. *$P<0.05$ for within treatment comparison between NAPSI=0 and NAPSI >0.

Statistical Analyses

In this post-hoc analyses, the number and percentage of patients achieving efficacy endpoints, including PASI 75/90/100 and sPGA (0,1)/(0), were summarized by severity of nail involvement category (with or without nail psoriasis; severe or mild nail psoriasis). Treatment-by-nail involvement inter-

FIGURE 2. Kaplan Meier curves showing time to achieve outcome in patients without (NAPSI=0) and with (NAPSI >0) nail psoriasis: (A) PASI 75, NAPSI=0 (B) PASI 75, NAPSI >0 (C) PASI 90, NAPSI=0 (D) PASI 90, NAPSI >0 (E) PASI 100, NAPSI=0 (F) PASI 100, NAPSI >0 (G) sPGA (0,1), NAPSI=0 (H) sPGA (0,1), NAPSI >0 (I) sPGA (0), NAPSI=0 (J) sPGA (0), NAPSI >0.



action was tested using a logistic model with treatment, nail involvement, and treatment-by-nail involvement interactions included in the model. Within each severity of nail involvement category, comparisons between treatment groups were made using the Cochran-Mantel-Haenszel (CMH) test stratified by study. Within each treatment group, comparisons between severities of nail involvement were also made using the CMH test. Missing data were imputed using non-responder imputation. In addition, Kaplan-Meier product limit method was used to estimate the time to first efficacy response, with treatment comparison done using a log-rank test stratified by study.

RESULTS

Of the 2570 patients with moderate-to-severe plaque psoriasis in the integrated dataset, 61.1% had fingernail involvement (NAPSI >0; n=1569), and 38.6% had severe nail psoriasis (NAPSI ≥16; n= 993) at baseline. Overall mean (SD) total scores at baseline were NAPSI 26.3 (20.1) (only those with nail involvement), PASI 20.3 (7.8), and sPGA 3.5 (0.6). Baseline characteristics were balanced across treatments (Table 1).

Significantly more patients treated with IXEQ2W and IXEQ4W achieved all endpoints starting as early as week 4 than those treated with ETN or PBO (P<0.05), regardless of nail psoriasis presence (Figure 1) or severity (Supplemental Figure 1). In the IXEQ2W treatment group, significantly more patients with nail psoriasis (NAPSI >0) than those without (NAPSI=0) achieved PASI 75 at week 8 (83.9% vs. 76.3%, *P*=0.01) and week 12 (91.1% vs 84.7%; *P*=0.008). Likewise, in the IXEQ2W treatment group, significantly more patients with severe nail psoriasis (NAPSI ≥16) compared with mild nail psoriasis (NAPSI <16) also achieved PASI 75 at week 8 (85.1% vs 78.4%; *P*=0.025) and week 12 (91.8% vs 86.5%; *P*=0.031). A similar percentage of patients in the IXEQ2W treatment group achieved PASI 90, PASI 100, sPGA (0,1), and sPGA (0) at all time points, regardless of nail psoriasis presence or severity.

In the IXEQ4W treatment group at week 12 (not an approved dose regimen in the US for moderate-to-severe psoriasis)[15] significantly more patients with nail psoriasis than without achieved sPGA (0,1) (76.9% vs. 70.1%; *P*=0.039), and a similar percentage of patients with severe and mild nail psoriasis achieved all endpoints. In the IXEQ4W treatment group, there were fluctuations in the response rates in patients without nail psoriasis who achieved PASI 100 and sPGA (0) that reached significance at week 4 (PASI 100 and sPGA [0]) and week 8 (PASI 100). However, by week 12 in both of these cases, there were numerically better responses in the patients with nail psoriasis.

In the ETN group, significantly more patients with severe nail psoriasis than with mild nail psoriasis achieved sPGA (0,1) at week 2 (3.6% vs 1.2%; *P*=0.017) (Supplemental Figure 1).

In both the IXEQ2W and IXEQ4W treatment groups, the Kaplan-Meier estimates for time to first response for PASI 75, PASI 90, PASI 100, sPGA (0,1), and sPGA (0) were all significantly earlier than either the PBO or ETN groups (*P*<0.001), regardless of nail psoriasis presence (Figure 2) or severity (Supplemental Figure 2). In both the IXEQ2W and IXEQ4W treatment groups, the Kaplan-Meier estimates for time to first response for PASI

TABLE 1.

Baseline Demographics and Clinical Characteristics (UNCOVER-2 and UNCOVER-3 Integrated Dataset, Intent-to-Treat Population)

	PBO N=361		ETN N=740		IXEQ4W N=733		IXEQ2W N=736		Total N=2570	
	NAPSI >0 N=227	NAPSI =0 N=134	NAPSI >0 N=461	NAPSI =0 N=279	NAPSI >0 N=445	NAPSI =0 N=288	NAPSI >0 N=436	NAPSI =0 N=300	NAPSI >0 N=1569	NAPSI = 0 N=1001
Age (years), mean (SD)[a]	46.2 (11.3)	45.4 (13.4)	46.3 (12.6)	44.3 (14.4)	45.7 (12.0)	44.6 (14.7)	45.5 (12.3)	44.4 (14.3)	45.9 (12.2)	44.6 (14.3)
Sex (male), n (%)	181 (79.7)	76 (56.7)	351 (76.1)	154 (55.2)	344 (77.3)	158 (54.9)	308 (70.6)	167 (55.7)	1184 (75.5)	555 (55.4)
Race (white), n (%)[a]	209 (92.1)	116 (86.6)	430 (93.7)	252 (91.0)	415 (93.7)	260 (90.9)	413 (94.9)	278 (92.7)	1467 (93.8)	906 90.9)
Weight [kg], mean (SD)[a]	93.7 (21.8)	87.4 (20.8)	93.2 (22.7)	91.3 (24.5)	93.2 (21.4)	89.7 (25.8)	90.4 (23.1)	88.9 (21.8)	92.5 (22.3)	89.6 (23.6)
≥100 kg, n (%)[a]	78 (34.5)	31 (23.5)	162 (35.1)	89 (32.0)	148 (33.3)	78 (27.6)	120 (27.5)	84 (28.1)	508 (32.4)	282 (28.4)
BMI [kg/m^2], mean (SD)[a]	30.8 (6.9)	30.1 (6.5)	30.7 (7.0)	31.4 (8.1)	30.6 (6.5)	30.6 (7.7)	30.0 (7.0)	30.3 (7.3)	30.5 (6.8)	30.7 (7.5)
% BSA, mean (SD)[a]	29.5 (19.5)	25.3 (13.9)	28.5 (18.2)	24.1 (13.0)	29.1 (17.7)	25.7 (15.3)	28.1 (18.8)	24.5 (12.6)	28.7 (18.4)	24.8 (13.7)
PASI score, mean (SD)[a]	21.4 (9.0)	19.9 (7.2)	20.7 (8.3)	18.6 (5.8)	21.4 (7.8)	19.4 (7.2)	21.1 (8.8)	18.6 (5.9)	21.1 (8.4)	19.0 (6.5)
sPGA score, mean (SD)[a]	3.6 (0.6)	3.5 (0.5)	3.6 (0.6)	3.4 (0.5)	3.6 (0.6)	3.5 (0.6)	3.6 (0.6)	3.4 (0.5)	3.6 (0.6)	3.5 (0.5)
NAPSI score, mean (SD)	26.5 (20.3)	0 (0)	27.6 (20.5)	0 (0)	25.0 (19.5)	0 (0)	26.3 (20.2)	0 (0)	26.3 (20.1)	0 (0)
Duration of psoriasis [years], mean (SD)[a]	19.8 (12.3)	16.6 (12.9)	19.3 (11.7)	17.1 (12.6)	19.5 (12.5)	16.9 (12.6)	19.2 (11.7)	16.5 (12.7)	19.4 (12.0)	16.8 (12.7)
Previous psoriasis treatment										
Non-biologic systemic only, n (%)[a,b]	85 (37.4)	48 (35.8)	208 (45.1)	103 (36.9)	199 (44.7)	114 (39.6)	187 (42.9)	111 (37.0)	679 (43.3)	376 (37.6)
Phototherapy (ever used), n (%)[c]	87 (38.3)	47 (35.1)	217 (47.1)	113 (40.5)	207 (46.5)	107 (37.2)	199 (45.6)	115 (38.3)	710 (45.3)	382 (38.2)
Biologics (ever used), n (%)[d]	48 (21.1)	28 (20.9)	77 (16.7)	59 (21.1)	87 (19.6)	56 (19.4)	82 (18.8)	60 (20.0)	294 (18.7)	203 (20.3)

BMI=body mass index, BSA=body surface area, ETN=etanercept; IXEQ2W=ixekizumab every 2 weeks; IXEQ4W=ixekizumab every 4 weeks; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index, PBO=placebo; SD=standard deviation; sPGA=static Physician's Global Assessment
[a]Percentages calculated for patients with available data
[b]Non-biologic systemic treatments included methotrexate, cyclosporine, retinoids, and psoralen and ultraviolet light A (PUVA); defined as any previous use of non-biologic systemic therapy
[c]Phototherapy included PUVA and ultraviolet light B (UVB) therapy; defined as any previous use of phototherapy
[d]Biologic treatments included efalizumab, ustekinumab, infliximab, alefacept, adalimumab, or golimumab; defined as any previous use of biologic therapy

75, PASI 90, PASI 100, sPGA (0,1), and sPGA (0) were all similar between patients, regardless of nail psoriasis presence or severity (P>0.05).

DISCUSSION

In this post-hoc analysis, ixekizumab was more effective than etanercept or placebo in clearance of plaque psoriasis in patients with or without concurrent nail involvement. Ixekizumab and etanercept were both effective in reducing signs and symptoms of nail and plaque psoriasis within 12 weeks.

Very few studies to date have compared treatment responses in patients with moderate-to-severe plaque psoriasis with and without nail psoriasis. One retrospective study examined 127 patients who were treated with topical therapy and one of four biologic treatments for 24 weeks: adalimumab, ustekinumab, etanercept, or infliximab. While all four biologic agents were effective in reducing nail and plaque psoriasis, patients with nail psoriasis had delayed skin clearance, with lower PASI 75 responses at weeks 8, 16, and 24 compared to patients without nail involvement.[8] Similarly, a post-hoc analysis of a randomized, controlled, phase 3 clinical trial of adalimumab (BELIEVE, NCT00574249) examined a subset of enrolled patients who had nail psoriasis at baseline. At all time points (weeks 2, 4, 8, 12, and 16), PASI 75 response was lower for patients with nail psoriasis (n=457) compared to those without (n=267).[9] In this report, there was no evidence to suggest nail involvement reduced the efficacy of ixekizumab treatment.

A challenge with all nail psoriasis treatments is the slow growth

of the nail plate. Optimal effect may take up to or exceed 52 weeks of therapy.[16] In UNCOVER-3, continued improvement of fingernail psoriasis was seen in patients treated with ixekizumab through 60 weeks.[12,14] Long-term efficacy and safety of ixekizumab for treatment of moderate-to-severe plaque psoriasis has been reported to 108 weeks.[17] Taken together, ixekizumab demonstrated early efficacy in fingernail psoriasis within 12 weeks and continued efficacy in open-label treatment to 60 weeks.

In conclusion, this study demonstrated that patients both with and without nail psoriasis responded well to ixekizumab. In contrast to previous reports in which the presence of nail psoriasis was a negative prognostic factor for psoriasis,[8,9] the presence of nail psoriasis did not negatively affect skin response in patients treated with ixekizumab.

DISCLOSURES

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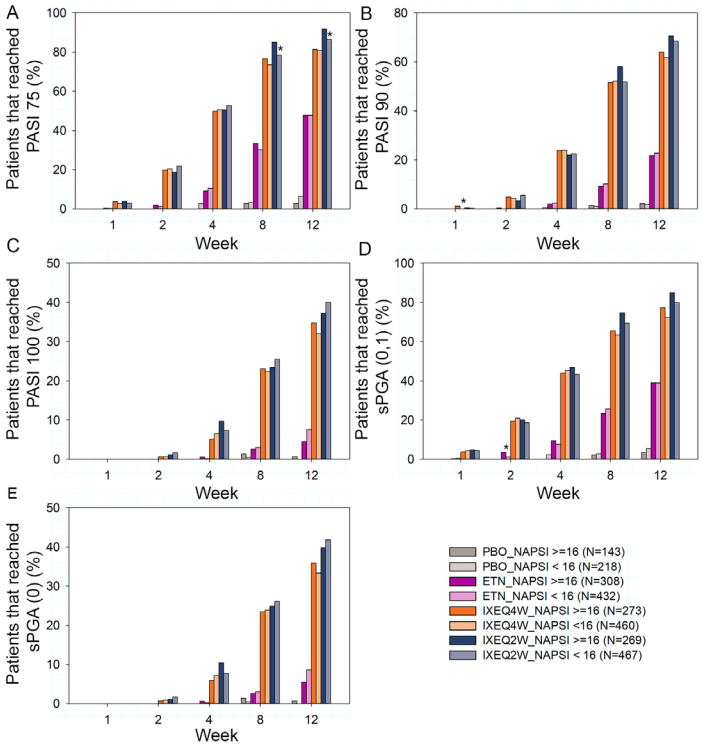
REFERENCES

1. Lowes MA, Bowcock AM , Krueger JG. Pathogenesis and therapy of psoriasis. *Nature.* 2007;445:866-873.
2. Kyriakou A, Patsatsi A, Sotiriadis D. Detailed analysis of specific nail psoriasis features and their correlations with clinical parameters: a cross-sectional study. *Dermatology.* 2011;223:222-229.
3. Klaassen KM, van de Kerkhof PC, Pasch MC. Nail psoriasis, the unknown burden of disease. *J Eur Acad Dermatol Venereol.* 2014;28:1690-1695.
4. Rigopoulos D, Baran R, Chiheb S, et al. Recommendations for the definition, evaluation, and treatment of nail psoriasis in adult patients with no or mild skin psoriasis: a dermatologist and nail expert group consensus. *J Am Acad Dermatol.* 2019;81:228-240.
5. Sobolewski P, Walecka I, Dopytalska K. Nail involvement in psoriatic arthritis. *Reumatologia.* 2017;55:131-135.
6. de Jong EM, Seegers BA, Gulinck MK, et al. Psoriasis of the nails associated with disability in a large number of patients: results of a recent interview with 1,728 patients. *Dermatology.* 1996;193:300-303.
7. Sanchez-Regana M, Sola-Ortigosa J, Alsina-Gibert M et al. Nail psoriasis: a retrospective study on the effectiveness of systemic treatments (classical and biological therapy). *J Eur Acad Dermatol Venereol.* 2011;25:579-586.
8. Bardazzi F, Lambertini M, Chessa MA, et al. Nail involvement as a negative prognostic factor in biological therapy for psoriasis: a retrospective study. *J Eur Acad Dermatol Venereol.* 2017;31:843-846.
9. Thaci D, Unnebrink K, Sundaram M, et al. Adalimumab for the treatment of moderate to severe psoriasis: subanalysis of effects on scalp and nails in the BELIEVE study. *J Eur Acad Dermatol Venereol.* 2015;29:353-360.
10. Gordon KB, Blauvelt A, Papp KA, et al; UNCOVER-1 Study Group; UNCOVER-2 Study Group; UNCOVER-3 Study Group. Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. *N Engl J Med.* 2016;375:345-356.
11. Griffiths CE, Reich K, Lebwohl M, et al; UNCOVER-2 and UNCOVER-3 investigators. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet.* 2015;386:541-551.
12. Dennehy EB, Zhang L, Amato D, et al. Ixekizumab is effective in subjects with moderate to severe plaque psoriasis with significant nail involvement: results from UNCOVER 3. *J Drugs Dermatol.* 2016;15:958-961.
13. Langley RG, Rich P, Menter A, et al. Improvement of scalp and nail lesions with ixekizumab in a phase 2 trial in patients with chronic plaque psoriasis. *J Eur Acad Dermatol Venereol.* 2015;29:1763-1770.
14. van de Kerkhof P, Guenther L, Gottlieb AB, et al. Ixekizumab treatment improves fingernail psoriasis in patients with moderate-to-severe psoriasis: results from the randomized, controlled and open-label phases of UNCOVER-3. *J Eur Acad Dermatol Venereol.* 2017;31:477-482.
15. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; 2019.
16. Elewski BE, Baker CS, Crowley JJ, et al. Adalimumab for nail psoriasis: efficacy and safety over 52 weeks from a phase-3, randomized, placebo-controlled trial. *J Eur Acad Dermatol Venereol.* 2019;33:2168-2178.
17. Blauvelt A, Gooderham M, Iversen L, et al. Efficacy and safety of ixekizumab for the treatment of moderate-to-severe plaque psoriasis: results through 108 weeks of a randomized, controlled phase 3 clinical trial (UNCOVER-3). *J Am Acad Dermatol.* 2017;77:855-862.

AUTHOR CORRESPONDENCE

Orin Goldblum MD
E-mail:.....goldblum_orin_m@lilly.com

SUPPLEMENTAL FIGURE 1. Proportion of patients achieving (A) PASI 75 (B) PASI 90 (C) PASI 100 (D) sPGA (0,1) or (E) sPGA (0) response through week 12 in patients with severe (NAPSI ≥16) and mild (NAPSI <16) nail psoriasis.



(A) Significantly more patients (P<0.05) treated with IXEQ4W and IXEQ2W with severe and mild nail psoriasis reached PASI 75 from week 1 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with severe and mild nail psoriasis reached PASI 75 from week 4 through 12 compared with PBO. (B) Significantly more patients treated with IXEQ4W and IXEQ2W with severe and mild nail psoriasis reached PASI 90 from week 2 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with severe and mild nail psoriasis reached PASI 90 from week 8 through 12 compared with PBO. (C) Significantly more patients treated with IXEQ2W with mild nail psoriasis reached PASI 100 at week 2 compared to ETN (P=0.007). Significantly more patients treated with IXEQ4W and IXEQ2W with severe and mild nail psoriasis reached PASI 100 from week 4 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with mild nail psoriasis reached PASI 100 at week 8 compared with PBO. Significantly more patients treated with ETN with severe and mild nail psoriasis reached PASI 100 at week 12 compared with PBO. (D) Significantly more patients treated with IXEQ4W and IXEQ2W with severe and mild nail psoriasis reached sPGA (0,1) from week 1 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with severe nail psoriasis reached sPGA (0,1) at week 2 compared with PBO. Significantly more patients treated with ETN with severe and mild nail psoriasis reached sPGA (0,1) at week 4 through 12 compared with PBO. (E) Significantly more patients treated with IXEQ2W with mild nail psoriasis reached sPGA (0) at week 2 compared to ETN (p=0.007). Significantly more patients treated with IXEQ4W and IXEQ2W with severe and mild nail psoriasis reached sPGA (0) from week 4 through 12 compared to PBO and ETN. Significantly more patients treated with ETN with mild nail psoriasis reached sPGA (0) at week 8 compared with PBO. Significantly more patients treated with ETN with severe and mild nail psoriasis reached sPGA (0) at week 12 compared with PBO.
*P<0.05 for within treatment comparison between NAPSI <16 and NAPSI ≥16.

SUPPLEMENTAL FIGURE 2. Kaplan Meier curves showing time to achieve outcome in patients with mild (NAPSI <16) and severe (NAPSI ≥16) nail psoriasis: (A) PASI 75, NAPSI <16 (B) PASI 75, NAPSI ≥16 (C) PASI 90, NAPSI <16 (D) PASI 90, NAPSI ≥16 (E) PASI 100, NAPSI <16 (F) PASI 100, NAPSI ≥16 (G) sPGA (0,1), NAPSI <16 (H) sPGA (0,1), NAPSI ≥16 (I) sPGA (0), NAPSI <16 (J) sPGA (0), NAPSI ≥16.