Comparison of Ixekizumab and Ustekinumab Efficacy in the Treatment of Nail Lesions of Patients With Moderate-to-Severe Plaque Psoriasis: 52-Week Data From the IXORA-S Trial

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BACKGROUND

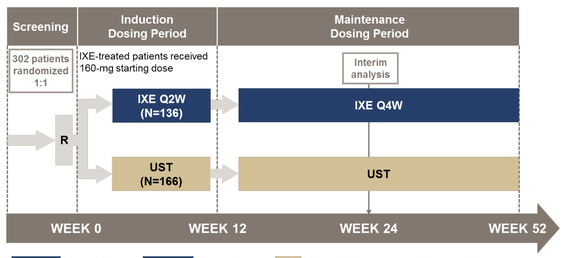
- Psoriasis is a chronic inflammatory disorder potentially affecting the skin, scalp, and nails1
- Up to 80% of patients with psoriasis have nail involvement1,2
- Nail psoriasis is persistent, slow to resolve, difficult to treat, and results can impair daily activities3-5
- IXORA-S is a Phase 3b, multicenter trial that compared the efficacy of ixekizumab with ustekinumab in patients with moderate-to-severe psoriasis
  - Ixekizumab demonstrated superior efficacy to ustekinumab in improving skin lesions up to Week 526 and nail psoriasis up to Week 247

OBJECTIVE

- To evaluate the comparative efficacy of ixekizumab and ustekinumab in the treatment of nail psoriasis in patients with moderate-to-severe psoriasis in the head-to-head IXORA-S study at 52 weeks

METHODS

Figure 1. Study Design: IXORA-S



IXE Q2W: 80 mg IXE every 2 weeks; IXE Q4W: 80 mg IXE every 4 weeks; UST: 45 mg UST for patients ≤100 kg and 90 mg UST for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

IXE=ixekizumab; R=randomization; UST=ustekinumab

- **Inclusion criteria**
  - ≥18-years-old
  - Chronic plaque psoriasis for ≥6 months prior to baseline
  - Failure, contraindication, or intolerance to ≥1 systemic therapya
  - Psoriasis Area and Severity Index (PASI) score ≥10 at screening and baseline
- **Exclusion criteria**
  - Pattern of pustular, erythrodermic, and/or guttate forms of psoriasis
  - History of drug-induced psoriasis
  - Received systemic non-biologic therapy or phototherapy for psoriasis <4 weeks before baseline, or have had topical psoriasis treatment <2 weeks before baseline
  - Concurrent or recent useb of any biologic agent prior to baseline

[a]Including cyclosporine, methotrexate, or phototherapy; [b]Within the following washout periods: etanercept <28 days; infliximab, adalimumab, or alefacept <60 days; golimumab <90 days; rituximab <12 months; or any other biologic agent <5 half-lives prior to baseline

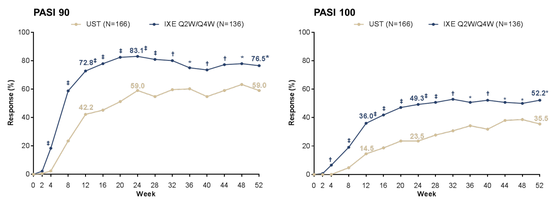
Statistical Analyses

- Categorical data
  - Logistic regression with terms for treatment, weight group (≤100 kg, >100 kg), and geographic region at Week 52
    - Fisher's exact test used as secondary analysis and at other visits
    - Missing data imputed using non-responder imputation
- Continuous data
  - Least squares mean change from baseline NAPSI and 95% confidence intervals for each treatment group compared using analysis of covariance with treatment, weight group (≤100 kg, >100 kg), geographic region, and baseline NAPSI score as factors
    - Missing data imputed using baseline observation for patients who discontinued due to adverse events
    - Last non-missing post-baseline observation carried forward used for patients discontinuing for other reasons (modified baseline observation carried forward)

RESULTS

Significantly More Ixekizumab-treated Patients Achieved PASI 90 and PASI 100 Versus Ustekinumab From Week 4 Through Week 52 (Primary Endpoint),[1] ITT Population, NRI

- Improvement of psoriasis was observed in both treatment groups



* p<.05 versus UST; † p≤.001 versus UST; ‡ p<.0001 versus UST based on Fisher's exact test

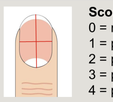
ITT=intent-to-treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; NRI=non-responder imputation; PASI 90/100=at least 90%/100% improvement in Psoriasis Area and Severity Index; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

1. Paul C, et al. *J Am Acad Dermatol.* 2018;S0190-9622:32195-32199.

Assessment of Nail Psoriasis

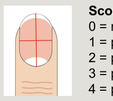
- The Nail Psoriasis Severity Index (NAPSI) was used to assess fingernail psoriasis in patients with fingernail psoriasis at baseline

Nail Matrix Psoriasis
Indicated by: pitting, leukonychia, red spots in the lunula, or nail plate crumbling



Score for Nail Matrix Psoriasis
0 = none
1 = present in 1/4 nail
2 = present in 2/4 nail
3 = present in 3/4 nail
4 = present in 4/4 nail

Nail Bed Psoriasis
Indicated by presence/absence of: onycholysis, splinter hemorrhages, oil drop, discoloration, or nail bed hyperkeratosis

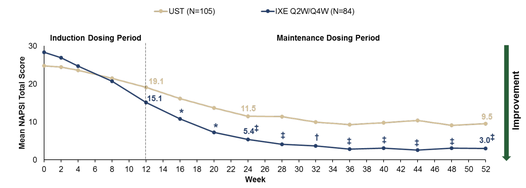


Score for Nail Bed Psoriasis
0 = none
1 = present in 1/4 nail
2 = present in 2/4 nail
3 = present in 3/4 nail
4 = present in 4/4 nail

Total for Each Nail_____(0-8)

NAPSI Total Score Was Significantly Improved as Early as Week 16 for Ixekizumab Versus Ustekinumab and Was Sustained Through Week 52, ITT Population With Baseline Fingernail Psoriasis, Observed

- Improvement of nail psoriasis was observed in both treatment groups

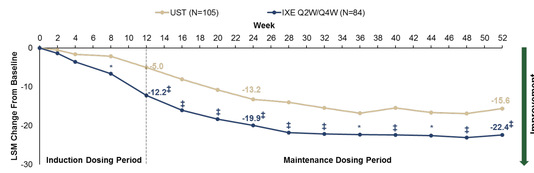


* p<.05; † p≤.001; ‡ p<.0001 IXE versus UST based on ANOVA with treatment, weight, geographic region, and baseline NAPSI score as factors

ANOVA=analysis of covariance; ITT=Intent-to-Treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; NAPSI=Nail Psoriasis Severity Index; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

Adjusted Change From Baseline in NAPSI Total Score Was Significantly Greater as Early as Week 8 for Ixekizumab Versus Ustekinumab and Was Sustained Through Week 52, ITT Population With Baseline Fingernail Psoriasis, mBOCF

- Improvement from baseline of nail psoriasis was observed in both treatment groups

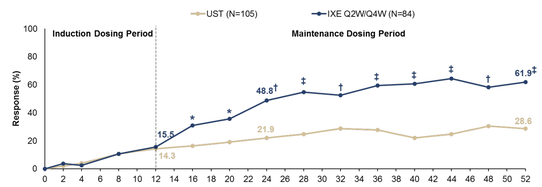


* p<.05; ‡ p<.0001 IXE versus UST based on ANOVA with treatment, weight, geographic region, and baseline NAPSI score as factors

ANOVA=analysis of covariance; ITT=Intent-to-Treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; LSM=least squares mean; mBOCF; modified baseline observation carried forward; NAPSI=Nail Psoriasis Severity Index; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

Significantly More Ixekizumab-treated Patients Achieved Complete Resolution of Nail Psoriasis Versus Ustekinumab From Week 16 Through Week 52, ITT Population With Baseline Fingernail Psoriasis, NRI

- Progressively more patients achieved complete resolution (NAPSI = 0) of nail psoriasis in both treatment groups



* p<.05; † p≤.001; ‡ p<.0001 IXE versus UST based on Fisher's exact test for treatment comparison

ITT=Intent-to-Treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; NAPSI=Nail Psoriasis Severity Index; NRI=non-responder imputation; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

CONCLUSIONS

- Improvement in nail psoriasis lesions was observed in both treatment groups in IXORA-S
- Complete resolution of nail psoriasis was seen in significantly greater percentages of patients treated with ixekizumab compared with ustekinumab from Week 16 through Week 52 of treatment
- Results suggest that ixekizumab provides significantly greater clearance of nail psoriasis than ustekinumab
- Longer periods of observation will be required to determine if nail lesions continue to improve beyond 52 weeks of treatment

Baseline Patient Demographics and Characteristics, ITT Population With Baseline Fingernail Psoriasis

	UST (N=105)	IXE Q2W/Q4W (N=84)
Age, years	45.4 (12.7)	43.0 (12.0)
Male, n (%)	80 (76.2)	60 (71.4)
Weight, kg	91.3 (24.4)	87.5 (21.7)
≤100 kg, n (%)	71 (67.6)	62 (73.8)
>100 kg, n (%)	34 (32.4)	22 (26.2)
NAPSI total score	24.8 (20.0)	28.3 (19.9)
Median	20.0	27.0
1st quartile	9.0	9.0
3rd quartile	34.0	43.5

Data are mean (standard deviation) unless otherwise specified

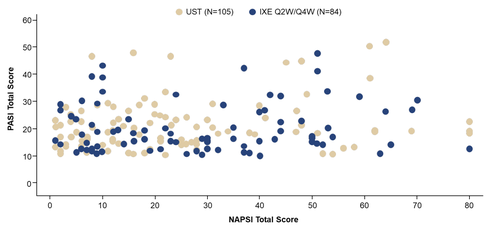
- 84 ixekizumab-treated (61.8%) and 105 ustekinumab-treated patients (63.3%) presented with fingernail psoriasis
- Baseline demographics and characteristics of patients were similar to those of patients in the ITT population[1]
  - No associations between treatment and age, gender, or weight found in patients with/without fingernail psoriasis at baseline

ITT=Intent-to-Treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; NAPSI=Nail Psoriasis Severity Index; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

1. Reich K, et al. *Br J Dermatol.* 2017;177:1014-1023.

Baseline NAPSI Score Was Not Correlated With Baseline PASI Score, ITT Population With Baseline Fingernail Psoriasis

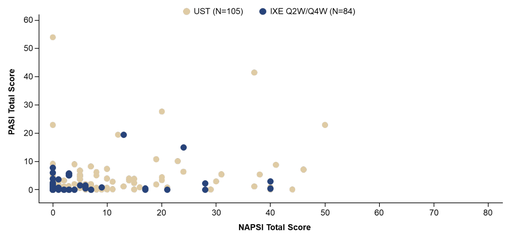
- No relationship between baseline NAPSI score and baseline PASI score was identified in either treatment group



ITT=intent-to-treat; IXE Q2W/Q4W=ixekizumab 80 mg every 2 weeks to Week 12 followed by ixekizumab 80 mg every 4 weeks; NAPSI=Nail Psoriasis Severity Index; PASI=Psoriasis Area and Severity Index; UST=45 mg ustekinumab for patients ≤100 kg and 90 mg ustekinumab for patients >100 kg at Weeks 0 and 4 and every 12 weeks thereafter per label

Patients Who Achieve Low PASI Scores at Week 52 May Still Experience Significant Nail Involvement at Week 52, ITT Population With Baseline Fingernail Psoriasis

- Most patients who have experienced nail improvement at Week 52 have also obtained low PASI



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Disclosures

- N. Wasel has provided consultancy services for: Abbott Laboratories, Amgen, Astellas Pharma, Biogen Idec, EMD Serono, Isotechnika, Janssen-Ortho, Ortho Biotech, Schering-Plough, and Wyeth, has performed contract research for: Abbott Laboratories, Amgen, Astellas Pharma, Biogen Idec, Celgene Corp, Centocor Ortho Biotech, Eli Lilly and Company, EMD Serono, Isotechnika, Leo Pharma, Merck Frosst, Novartis Pharmaceuticals, Pfizer, Takeda, and Wyeth; Y. Dutronc is a current employee and stockholder of Eli Lilly and Company; B. Schinzel worked as a freelancer for Clinipace Worldwide to conduct the analysis of this study; J-P Lacour has received grants from: AbbVie, Boehringer, Celgene, Eli Lilly and Company, Janssen, Leo Pharma, Novartis, and Roche, has been a consultant for: AbbVie, Celgene, Eli Lilly and Company, Leo Pharma, and Novartis
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