Ixekizumab Demonstrates Comprehensive Psoriasis Clearance in Patients With Moderate-to-Severe Psoriasis With Scalp, Nail, and/or Palmoplantar Involvement: UNCOVER-1, -2 Trials Through 5 Years

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BACKGROUND

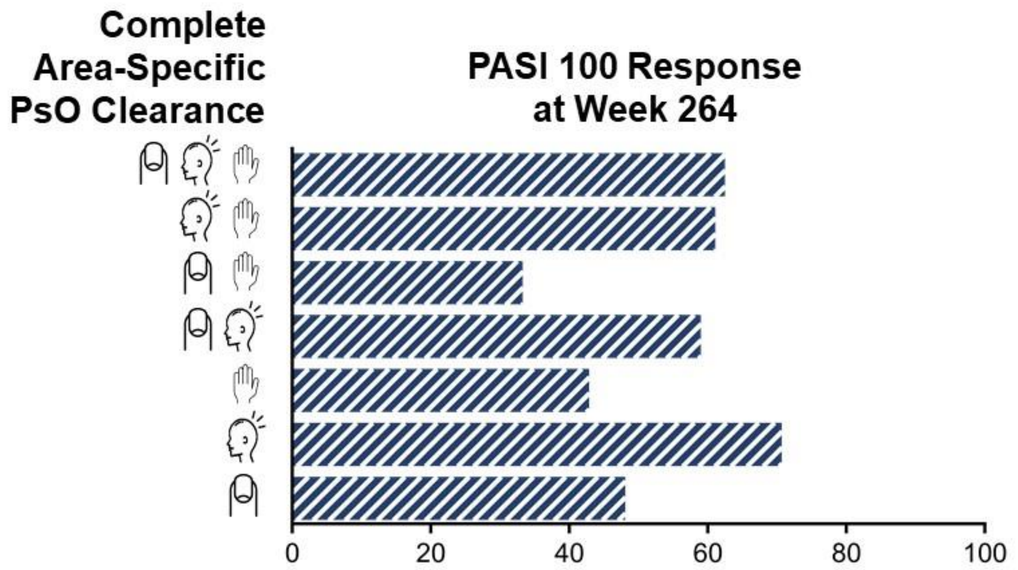
- Ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A,[1] has been approved for the treatment of moderate to severe psoriasis (PsO) in adult and pediatric populations
- Involvement of challenging body areas (area-specific clearance of scalp, nails, and palmoplantar areas) is an important treatment consideration because patients with PsO in these areas can have disproportionately greater burden of disease
- UNCOVER-1 (NCT01474512) and UNCOVER-2 (NCT01597245) are randomized, double-blind, multicenter, Phase 3 clinical trials of ixekizumab for the treatment of moderate to severe plaque PsO[2]

OBJECTIVE

- To assess comprehensive clearance by measuring the ability of ixekizumab to achieve complete skin clearance (100% improvement from baseline in Psoriasis Area and Severity Index [PASI 100]) for up to 5 years when multiple challenging body areas (scalp, nails, and palmoplantar areas) are involved

SUMMARY OF KEY FINDINGS

PASI 100 response was maintained for up to **5 years** in patients with PsO treated with IXE who achieved area-specific PsO clearance for nail, scalp, and/or palmoplantar areas



CONCLUSIONS

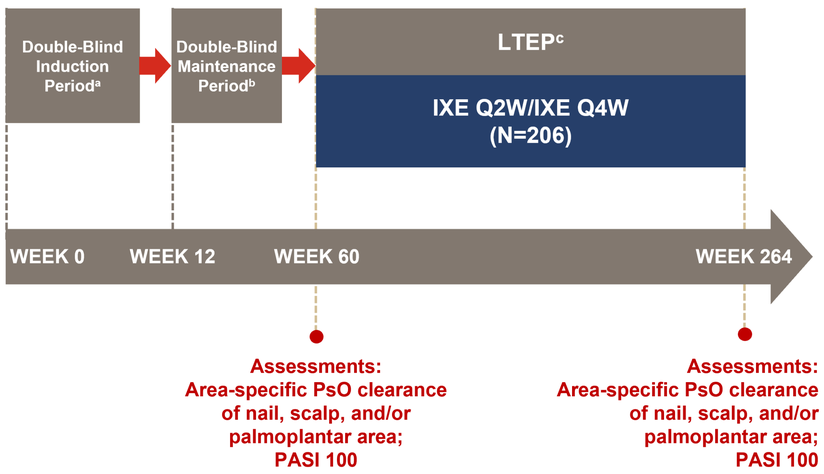
- PsO involvement across multiple challenging body areas may be more difficult to treat
- Of patients who achieved complete area-specific PsO clearance of nail, scalp, and/or palmoplantar areas at Week 60 with ixekizumab, a majority also achieved PASI 100 at Week 60
- PASI 100 responses were sustained through Week 264 (5 years) of ixekizumab treatment
- Ixekizumab provides benefits for patients with PsO for up to 5 years, even when multiple challenging body areas are involved concurrently

Limitation

- Small sample sizes in subgroups

METHODS

Study Design, UNCOVER-1/-2 Long-Term Extension Period



[a] Week 0: UNCOVER-1 patients were randomized to IXE Q2W, IXE Q4W, or PBO; UNCOVER-2 patients were randomized to IXE Q2W, IXE Q4W, etanercept, or PBO; [b] Week 12: sPGA (0,1) responders (clear or minimal plaque PsO) were randomized to IXE Q4W, IXE Q12W, or PBO; [c] From Weeks 60-264, patients and Investigators could elect to escalate from IXE Q4W to IXE Q2W dosing through the end of the study to achieve or maintain efficacy (23 patients in UNCOVER-1 and 20 patients in UNCOVER-2)

Key Eligibility Criteria

Inclusion

- ≥18 years of age with moderate to severe plaque PsO
- PASI ≥12 at screening and baseline visits
- ≥10% body surface area affected at screening and baseline visits
- Static Physician's Global Assessment score ≥3

Assessments

PASI 100: Complete skin clearance assessed at Weeks 60 and 264 in patients who achieved clearance of nail, scalp, and/or palmoplantar areas

Statistical Analyses

- Analyses included participants who received the approved-label dose of ixekizumab every 2 weeks (Q2W) during the first 12 weeks and every 4 weeks after Week 12 through the Maintenance Period (Weeks 12-60) and continued in the Long-Term Extension Period (Weeks 60-264), excluding data from visits with titrated Q2W long-term dosing
- Participants were analyzed by area-specific involvement at baseline:
  - Nail (Nail Psoriasis Severity Index [NAPSI], N=123)
  - Scalp (Psoriasis Scalp Severity Index [PSSI], N=189)
  - Palmoplantar (Palmoplantar PASI [PPASI], N=57)
  - Nail and scalp (NAPSI+PSSI, N=115)
  - Nail and palmoplantar (NAPSI+PPASI, N=50)
  - Scalp and palmoplantar (PSSI+PPASI, N=55)
  - Nail, scalp, and palmoplantar (NAPSI+PSSI+PPASI, N=50)
- PASI 100 was assessed for subsets of patients who had area-specific involvement at baseline and achieved complete PsO clearance of that area at Weeks 60 and 264
- Observed data were summarized using descriptive statistics

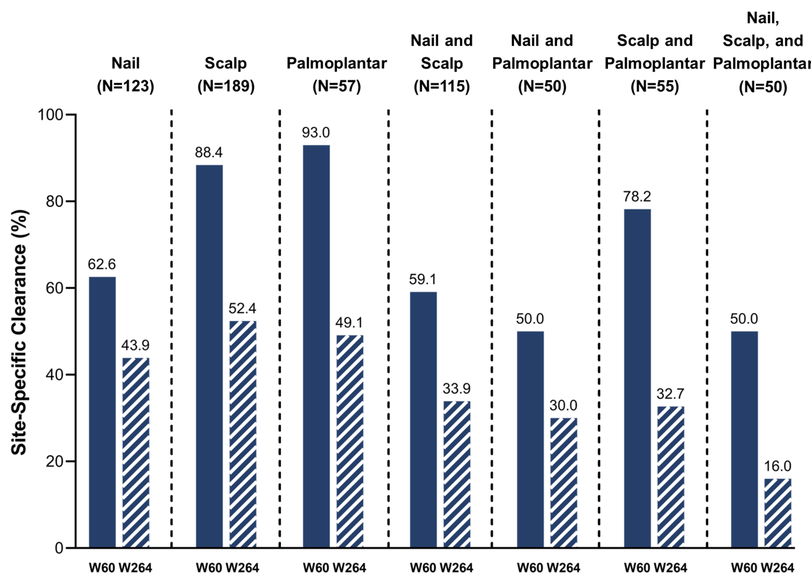
RESULTS

Demographics and Baseline Characteristics in Patients With Area-Specific Baseline PsO Involvement

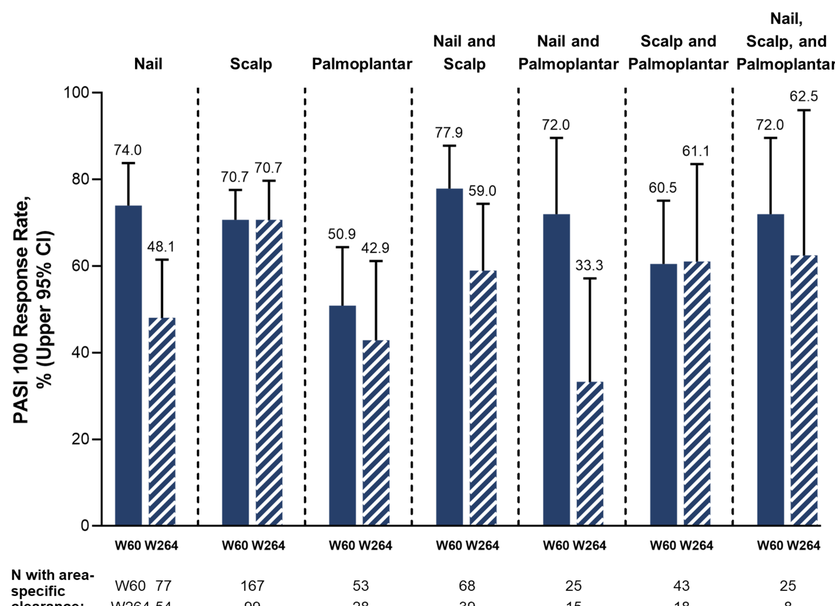
	Nail (N=123)	Scalp (N=189)	Palmoplantar (N=57)	Nail and Scalp (N=115)	Nail and Palmoplantar (N=50)	Scalp and Palmoplantar (N=55)	Nail, Scalp, and Palmoplantar (N=50)
Age, years	44.8 (12.2)	43.4 (12.8)	48.2 (11.4)	44.5 (12.0)	48.7 (11.2)	48.4 (11.2)	48.7 (11.2)
Male, n (%)	90 (73.2)	126 (66.7)	46 (80.7)	83 (72.2)	40 (80.0)	44 (80.0)	40 (80.0)
Duration of PsO symptoms, years	19.3 (11.8)	18.4 (12.1)	21.6 (12.0)	19.3 (11.5)	21.4 (11.3)	21.4 (11.3)	21.4 (11.3)
Age of PsO onset, years	25.9 (12.6)	25.4 (12.4)	27.0 (13.7)	25.7 (12.5)	27.7 (14.0)	27.5 (13.6)	27.7 (14.0)
% BSA involvement	28.8 (18.3)	27.4 (16.4)	33.6 (21.7)	29.0 (18.5)	33.1 (21.8)	33.8 (21.8)	33.1 (21.8)
Itch NRS	6.6 (2.6)	6.8 (2.5)	7.2 (2.1)	6.7 (2.5)	7.2 (2.1)	7.2 (2.2)	7.2 (2.1)
PASI	20.0 (7.9)	19.5 (7.0)	22.0 (9.2)	20.2 (8.1)	22.3 (9.5)	22.3 (9.3)	22.3 (9.5)

Data are mean (standard deviation) unless stated otherwise

Complete Area-Specific PsO Clearance at Weeks 60 and 264 in Patients With Baseline Nail, Scalp, or Palmoplantar Involvement



PASI 100 Response Rate at Weeks 60 and 264 in Patients With Complete Area-Specific Nail, Scalp, or Palmoplantar Clearance



DISCLOSURES

- **A. B. Gottlieb** has received honoraria as an advisory board member and consultant for: Amgen, AnaptysBio, Avotres, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Janssen, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and XBiotech (stock options for an RA project); and has received research and/or educational grants from: AnapytysBio, Janssen, Novartis, Ortho, Sun Pharma, and UCB Pharma (all funds go to Mount Sinai Medical School); **J. F. Merola** is a consultant and/or investigator for: AbbVie, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, EMD Serono, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; **N. Somani**, **B. Konicek**, **K. See**, and **G. Gallo** are employees and shareholders of: Eli Lilly and Company; **M. McKean-Matthews** is an employee of: Syneos Health working on behalf of Eli Lilly and Company; **P. Rich** has received grants from: Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, Galderma, Janssen Ortho, Kadmon, Moberg Derma, Novartis, Pfizer, Sun Pharma, and UCB Pharma
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ABBREVIATIONS

BSA=body surface area; CI=confidence interval; IXE=ixekizumab; IXE Q2W=80 mg IXE every 2 weeks; IXE Q4W=80 mg IXE every 4 weeks; IXE Q12W=80 mg IXE every 12 weeks; LTEP=Long-Term Extension Period; NAPSI=Nail Psoriasis Severity Index; NRS=numeric rating scale; PASI=Psoriasis Area and Severity Index; PASI 100=100% improvement from baseline in PASI; PBO=placebo; PPASI=Palmoplantar PASI; PsO=psoriasis; PSSI=Psoriasis Scalp Severity Index; sPGA=static Physician's Global Assessment; W=Week

REFERENCES

1. Liu L, et al. *J Inflamm Res*. 2016;9:39-50.
2. Gordon KB, et al. *N Engl J Med*. 2016;375:345-356.

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