# Ixekizumab vs. Guselkumab: Direct Comparison of Cumulative Clinical and Quality of Life Benefits Over 24 Weeks of Treatment in Patients With Moderate-to-Severe Plaque Psoriasis

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## BACKGROUND

- Ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin (IL)-17A,[1] has been approved for treating moderate-to-severe psoriasis (PsO), active psoriatic arthritis, and ankylosing spondylitis
- IXORA-R (NCT03573323) is a Phase 4, randomized, double-blind, head-to-head, multicenter trial comparing the efficacy and safety of ixekizumab with guselkumab, an IL-23p19 inhibitor, in patients with moderate-to-severe plaque PsO
  - Significantly more patients treated with ixekizumab vs. guselkumab achieved complete skin clearance following 12 weeks of treatment[2]
  - Significantly more patients treated with ixekizumab vs. guselkumab achieved Psoriasis Area Severity Index (PASI) 50 at Week 1, PASI 75 at Week 2, and PASI 100 at Week 4[2]
- Conventional measurements for assessing PsO treatment effects capture improvements at fixed, prespecified time points and fail to account for cumulative clinical benefits over time

## OBJECTIVE

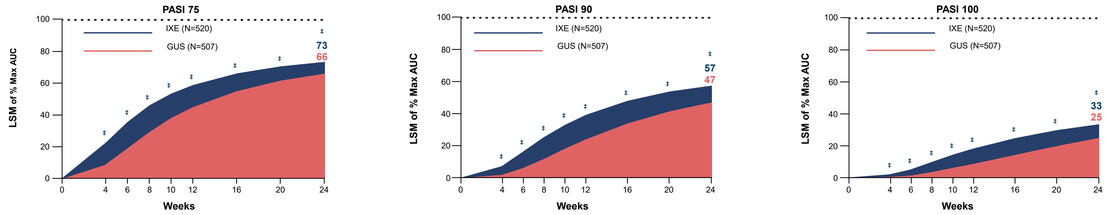
- The objective of this post hoc analysis was to compare the cumulative benefits of ixekizumab vs. guselkumab over 24 weeks of treatment with respect to skin clearance, itching, and health-related quality of life (HRQoL)

## CONCLUSION

- Patients treated with ixekizumab demonstrated greater cumulative benefit over 24 weeks compared with guselkumab
  - More rapid and sustained efficacy was shown across PASI response categories
  - More days of complete skin clearance
  - Greater improvements in HRQoL and itch

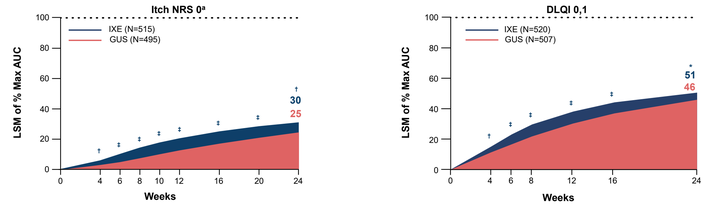
## KEY RESULTS

### PASI 75/90/100 Cumulative (AUC) Curves



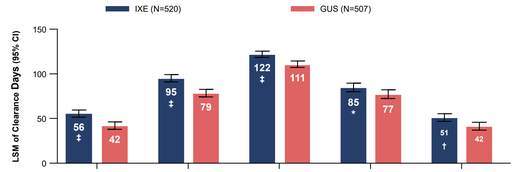

‡ p<.001 vs. GUS, nominal p-values

### Itch NRS (0) and DLQI (0,1) Cumulative (AUC) Curves




[a] Patients with baseline Itch NRS >0; IXE (N=515); GUS (N=495)
* p<.05; † p<.01; ‡ p<.001 vs. GUS, nominal p-values

### Number of Improved Skin Clearance Days Through Week 24




[a] Patients with baseline Itch NRS >0; IXE (N=515); GUS (N=495)
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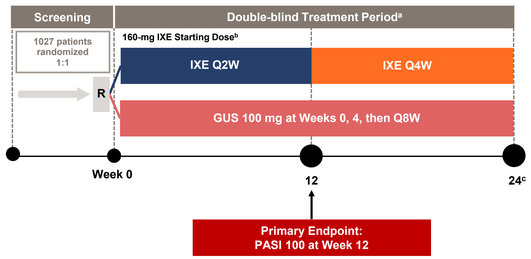
## METHODS

### Study Design, IXORA-R




[a] Patients received approved label dose for PsO for IXE and GUS; [b] Administered as two 80-mg injections at Week 0; [c] After Week 24, patients entered a post-treatment follow-up period for a minimum of 12 weeks (maximum follow-up 24 weeks to Week 48)

### Key Eligibility Criteria

**Inclusion**

- ≥18 years old with chronic plaque PsO for ≥6 months prior to baseline
- Static Physician's Global Assessment score of ≥3 at screening and at baseline
- PASI score ≥12 at screening and at baseline
- ≥10% body surface area involvement at screening and at baseline

**Exclusion**

- Previous treatment with IL-23p19 antagonists
- Previous treatment with ixekizumab or failure to respond to an IL-17 antagonist
- Concurrent or recent use of any biologic agent within the specified periods prior to baseline[a]
- Had a clinically significant flare of PsO during the 12 weeks before baseline

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

### Outcome Measures

**Plaque PsO**
PASI 75/90/100 response
Weeks 1, 2, 4, 6, 8, 10, 12, and every 4 weeks

**HRQoL**
DLQI (0,1) response
Weeks 2, 4, 6, 8, 12, 16, and 24
Score of 0 or 1=no effect of PsO on HRQoL

**Itch**
Itch NRS (0) response
Weeks 1, 2, 4, 6, 8, 10, 12, and every 4 weeks
Score of 0=no itch

**Cumulative Benefit of Each Outcome**
AUC of response rate over time through Week 24

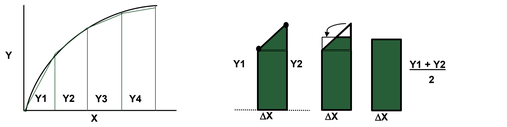
### Baseline Demographics

| | IXE (N=520) | GUS (N=507) |
|---|---|---|
| **Age, years** | 49.0 (13.9) | 49.0 (14.9) |
| **Male, n (%)** | 338 (65) | 314 (62) |
| **Weight, kg** | 96.6 (24.9) | 94.6 (24.9) |
| **Duration of PsO since diagnosis, years** | 17.5 (13.8) | 16.3 (13.8) |
| **% BSA** | 24.1 (16.1) | 23.8 (15.4) |
| **PASI** | 19.5 (7.9) | 19.3 (7.1) |
| **DLQI** | 12.8 (6.9) | 13.2 (7.4) |
| **Itch NRS** | 6.9 (2.4) | 7.1 (2.5) |
| **Prior PsO therapy, n (%)** | | |
| **Nonbiologic systemic** | 170 (33) | 141 (28) |
| **Topical therapy** | 375 (72) | 354 (70) |
| **Phototherapy** | 77 (15) | 63 (12) |
| **Biologic** | 139 (27) | 134 (26) |

Data are mean (standard deviation) unless otherwise stated

### Statistical Analysis

- Missing data were imputed using non-responder imputation
- Cumulative clinical benefits of ixekizumab and guselkumab were calculated post hoc by evaluating the area under the curve (AUC) for responders of PASI 75/90/100, Dermatology Life Quality Index (DLQI [0,1]), and Itch numeric rating scale (NRS)=0
  - AUC over 24 weeks ($AUC_{0\text{-}24\ wks}$) was determined using the trapezoidal rule, which approximates the area using a series of trapezoids:




  - Treatment differences in normalized AUC (percent of maximum AUC) were compared using the analysis of covariance model after adjusting for baseline values and pooled sites
  - The number of average days for achieving PASI 75/90/100 skin clearance, DLQI (0,1), and Itch NRS=0 over 24 weeks were estimated based on the percentage of the maximum AUC and the study duration
  - Normalized AUC: data were normalized and expressed as a percentage of maximum possible AUC

DISCLOSURES

**A. Blauvelt** has served as a scientific adviser and/or clinical study investigator for: AbbVie, Aclaris, Almirall, Arena Pharmaceuticals, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, FLX Bio, Forté Pharma, Galderma, Incyte, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma; and as a paid speaker for: AbbVie; **K. A. Papp** has served as a speaker and/or adviser and/or received grant/research support from: AbbVie, Akros Pharma, Amgen, Anacor Pharmaceuticals, Arcutis, Astellas, AstraZeneca, Baxalta, Baxter International, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite BioPharma, Coherus BioSciences, Dermira, Dow Pharmaceutical, Eli Lilly and Company, Forward Pharma, Galderma, Genentech, Gilead Sciences, GlaxoSmithKline, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, MedImmune, Meiji Seika Pharma, Merck Serono, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB Pharma, and Valeant/Bausch Health; **M. Gooderham** has received honoraria, grants, and/or research funding as a speaker, investigator, advisory board member, data safety monitoring board member, and/or consultant for: AbbVie, Akros Pharma, Amgen, Arcutis, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Valeant; **N. J. Korman** has received honoraria, grants, and/or research funding as a speaker, investigator, advisory board member, and/or consultant for: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Immune Tolerance, Janssen, Kyowa Kirin, LEO Pharma, Menlo Therapeutics, Merck, Novartis, Pfizer, Principia Biopharma, Prothena, Regeneron, Rhizen Pharmaceuticals, Sanofi Genzyme, Sun Pharma, Syntimmune, Trevi Therapeutics, UCB Pharma, Valeant, and XBiotech; **R. Vender**, **R. Burge**, **B. Zhu**, **G. Gallo**, **S. Y. Park**, **H. ElMaraghy**, **F. Wang**, **R. G. Lima**, and **L. Renda** are employees and shareholders of: Eli Lilly and Company

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ABBREVIATIONS

*AUC=area under the curve; BSA=body surface area; CI=confidence interval; DLQI=Dermatology Life Quality Index; GUS=guselkumab; HRQoL=health-related quality of life; IL=interleukin; IXE=ixekizumab; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; LSM=least square mean; Max=maximum; NRS=numeric rating scale; PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/≥90%/100% response; PsO=psoriasis; Q8W=every 8 weeks; R=randomization*

REFERENCES

1.Liu L, et al. *J Inflamm Res*. 2016;9:39-50.
2.Blauvelt A, et al. *Br J Dermatol*. 2020;182:1321-1322.



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