Treatment of Plaque Psoriasis Involving High-Impact Sites With Icotrokinra: Subgroup Analyses of the Phase 3, ICONIC-LEAD Trial

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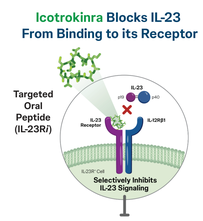
Background

- Plaque psoriasis (PsO) involving difficult-to-treat sites (e.g., scalp, genitals, palms/soles, nails) can highly impact patients
- Current treatment guidelines include PsO patients with high-impact site involvement as candidates for systemic therapy, regardless of body surface area (BSA) affected[1]

Icotrokinra (ICO)

- Targeted oral peptide that selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[2]
- Demonstrated significantly higher skin response rates and similar adverse event (AE) rates vs placebo (PBO) at Week (W)16, and no safety signals through W24, in adults & adolescents with moderate-to-severe plaque PsO (ICONIC-LEAD)[3]
- Showed significant skin clearance, including in the scalp and genital areas, and generally similar AE rates, vs PBO at W16 in participants (pts) with plaque PsO involving high-impact sites (ICONIC-TOTAL)[4]

Icotrokinra Blocks IL-23 From Binding to its Receptor



IFN=interferon, *IL-12Rβ1*=interleukin-12 receptor beta 1, *IL-23R*=interleukin-23 receptor, *IL-23Ri*=interleukin-23 receptor inhibitor.

Objective

Evaluate the effect of ICO in subsets of ICONIC-LEAD pts with PsO involving difficult-to-treat, high-impact sites, including the scalp, genitals, hands/feet, and nails through W24

Methods

ICONIC-LEAD Key Inclusion Criteria

Moderate-to-severe plaque PsO (N=684)

- ≥12 years
- Plaque PsO for ≥26 weeks
- BSA ≥10%
- PASI score ≥12
- IGA score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO

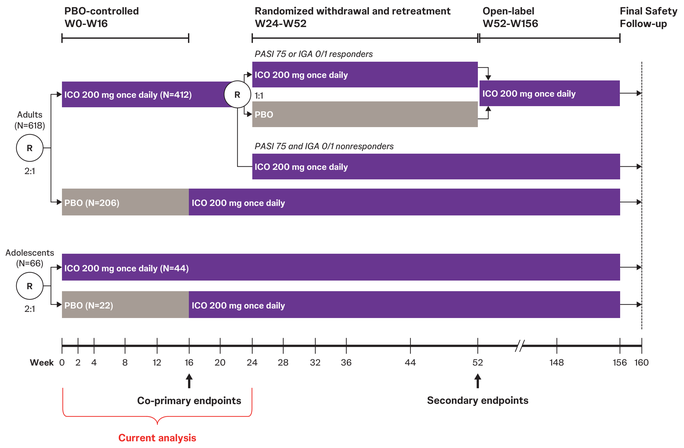
IGA=Investigator's Global Assessment, *PASI*=Psoriasis Area and Severity Index.

Outcomes & Analyses

ICO vs PBO at W16 and ICO at W24

- Scalp-specific IGA (ss-IGA) score of 0/1 and 0[a]
- Static Physician's Global Assessment of Genitalia (sPGA-G) score of 0/1 and 0[a]
- PGA of hands and feet (hf-PGA) score of 0/1 and 0[a]
- Fingernail PGA (f-PGA) score of 0/1 and 0[a]
- Modified Nail Psoriasis Severity Index (mNAPSI) percent improvement from baseline[b]

[a]Nonresponder imputation/[b]zero percent improvement from baseline assigned after pts discontinued study drug due to a lack of efficacy or an AE of worsening of PsO, or initiated prohibited medication that could impact PsO. Observed data were used for pts who discontinued study agent for other reasons.
[c]After accounting for these intercurrent events, pts with missing data were considered nonresponders. [d]The remaining missing data were not imputed and were accounted for through correlation of repeated measure in the *MMRM* model. ***MMRM***=mixed-effect model repeated measure.



Key Takeaways

In ICONIC-LEAD, a pivotal phase 3 study evaluating the targeted oral peptide ICO in pts with moderate-to-severe plaque PsO and high-impact site involvement:

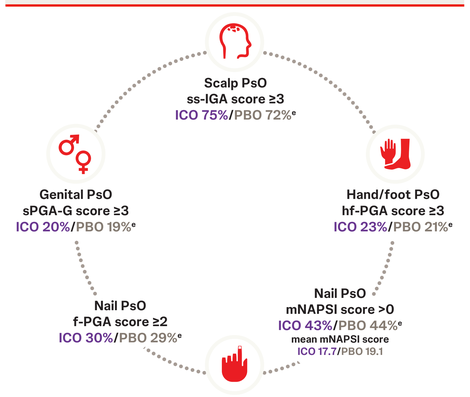
- **ICO demonstrated higher rates of scalp, genital, and hand/foot PsO clearance vs PBO at W16**
  - ✓ **Approximately 80% of ICO-treated pts achieved clear/almost clear – and 62-70% achieved completely clear – high-impact site PsO at W24**
- **ICO substantially improved nail PsO at W16, an early timepoint for nail assessment**
  - ✓ **Approximately 30% of ICO-treated pts achieved completely clear nail PsO at W24**

Results

Baseline characteristics were similar between groups

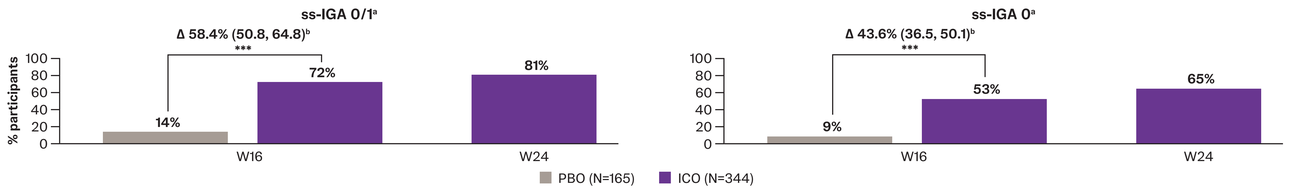
Baseline Characteristics	ICO 200 mg QD (N=456)	PBO (N=228)
Demographics		
Age, yrs	42.4 (16.3)	43.2 (16.6)
Female	36%	32%
Race, Asian/Black/White	24/1/72%	25/1/72%
BMI, kg/m^2	29.2 (6.9)[a]	29.3 (7.0)[a]
Disease Characteristics		
PsO disease duration, yrs	17.3 (13.9)	16.6 (12.7)
% BSA with PsO	24.6 (14.3)	27.1 (16.2)
IGA score		
Moderate (3)	75%	76%
Severe (4)	25%	24%
PASI (0-72)	19.4 (7.1)	20.8 (8.1)
Prior PsO treatments		
Phototherapy[b]	30%	29%
Systemic therapy[c]	72%	71%
Biologic therapy[d]	32%	37%

High-impact site PsO was balanced between groups



*Data shown are mean (SD) unless otherwise noted. PsO involving high-impact sites was not mutually exclusive. [a]ICO: N=455; PBO: N=227. [b]PUVA and UVB. [c]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [d]Adalimumab, difepacept, bimekizumab, certolizumab pegol, efalizumab, etanercept, guselkumab, ixifimab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. [e]Among all randomized pts (ICO N=456/PBO N=228). **BMI**=body mass index, **PUVA**=psoralen plus ultraviolet A, **QD**=once daily, **SD**=standard deviation, **UVB**=ultraviolet B.*

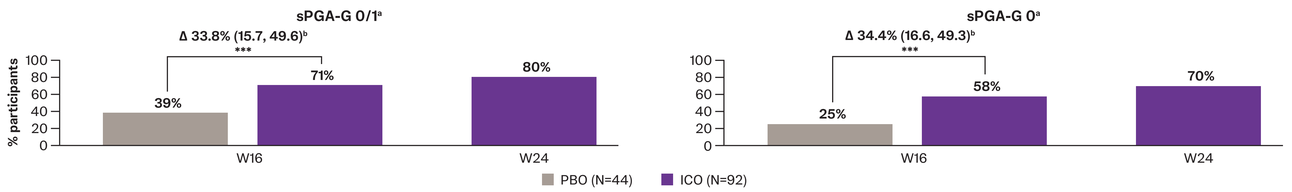
ICO demonstrated high rates of scalp PsO clearance at W16 & W24



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[c]

*[a]Among pts with a baseline ss-IGA score ≥3. [b]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for age group, baseline weight category for adults, and geographic region using Mantel-Haenszel weights. [c]P-values were based on CMH chi-square test stratified by age group, baseline weight category for adults, and geographic region. **CI**=confidence interval, **CMH**=Cochran-Mantel-Haenszel.*

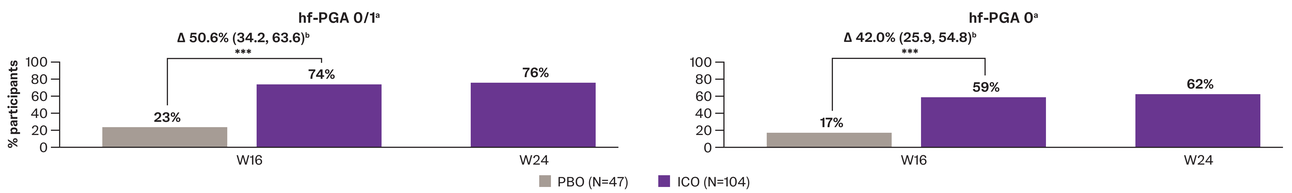
Substantial proportions of ICO-treated pts achieved genital PsO clearance at W16 & W24



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[c]

[a]Among pts with a baseline sPGA-G score ≥3. [b]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for age group and baseline weight category for adults using Mantel-Haenszel weights. [c]P-values were based on CMH chi-square test stratified by age group and baseline weight category for adults.

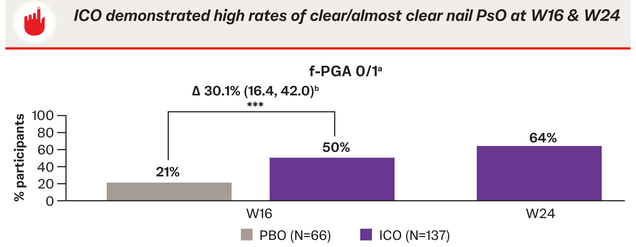
ICO cleared hand/foot PsO at high rates at W16 & W24



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[c]

[a]Among pts with a baseline hf-PGA score ≥3. [b]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for age group and baseline weight category for adults using Mantel-Haenszel weights. [c]P-values were based on CMH chi-square test stratified by age group and baseline weight category for adults.

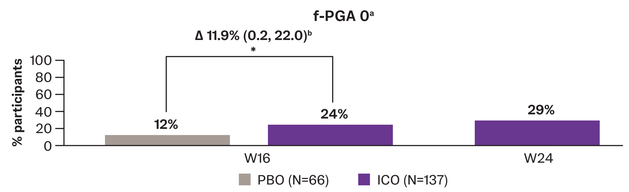
ICO demonstrated high rates of clear/almost clear nail PsO at W16 & W24



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[c]

[a]Among pts with a baseline f-PGA score ≥2. [b]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for age group and baseline weight category for adults using Mantel-Haenszel weights. [c]P-values were based on CMH chi-square test stratified by age group and baseline weight category for adults.

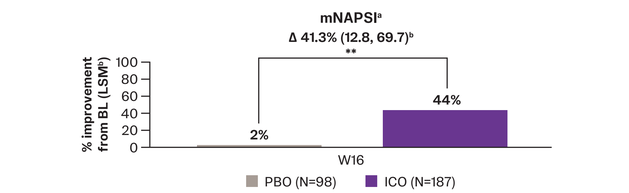
Nearly 30% of ICO-treated pts achieved completely clear nail PsO at W24



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[c]

[a]Among pts with a baseline f-PGA score ≥2. [b]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for age group and baseline weight category for adults using Mantel-Haenszel weights. [c]P-values were based on CMH chi-square test stratified by age group and baseline weight category for adults.

ICO-treated pts achieved substantial improvement in mNAPSI at W16



Nominal **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO[b]

*[a]Among pts with a baseline mNAPSI score >0. [b]LS Mean, LS Mean difference, and p-value were based on the MMRM model with treatment group, visit, treatment group by visit interaction, age group, baseline weight, geographic region, baseline mNAPSI total score, and baseline mNAPSI total score by visit interaction as covariates. **BL**=baseline, **LSM**=least squares mean.*

PRESENTED AT: Dermatology Innovation Symposium; August 8-10, 2025; Anaheim, CA, USA. **PREVIOUSLY PRESENTED AT:** AAD Innovation Academy; July 10-13, 2025; Chicago, IL, USA.
REFERENCES: 1. Strober B. *J Am Acad Dermatol.* 2020;82:117-22. **2.** Fourie AM. *Sci Rep.* 2024;14:17515. **3.** Bissonnette R. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA. **4.** Gooderham MJ. SID Annual Meeting; May 7-10, 2025; San Diego, CA, USA.
ACKNOWLEDGMENTS: Medical writing support was provided by R. Contento, PharmD, of Johnson & Johnson under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022:175:1298-1304). This presentation was sponsored by Johnson & Johnson.
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