High-Level Improvements in Psoriasis Area and Severity Index With Icotrokinra in Participants With Moderate-to-Severe Plaque Psoriasis: Results Through Week 24 of the Phase 3 ICONIC-LEAD Study

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Background

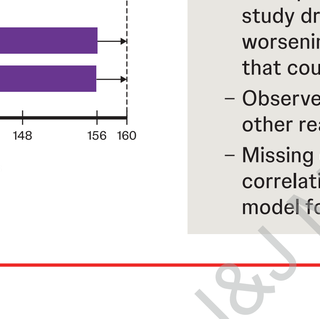
Psoriasis (PsO) Treatment Goals

- Early and sustained improvements in the extent and severity of PsO are important treatment goals, with achievement of an absolute Psoriasis Area and Severity Index (aPASI) threshold ≤2 considered a clinically relevant treatment target[1]
- An aPASI ≤3 achieved within the initial 3-4 months of treatment is also considered an acceptable treat-to-target strategy[2]

Icotrokinra (ICO)

- First-in-class targeted oral peptide that selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[3]
- Demonstrated significantly higher rates of skin clearance 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)[4]

Icotrokinra Blocks IL-23 From Binding to its Receptor



Inhibits IL-17A, IL-17F, IL-22, and IFNγ Production

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

Objectives

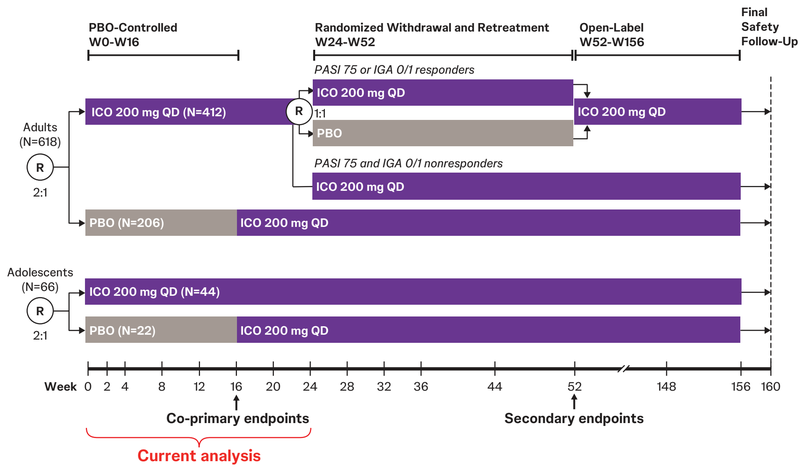
Evaluate ICO effect on relative PASI improvements and achievement of aPASI thresholds, including those associated with treatment targets, through W24 in ICONIC-LEAD participants (pts)

ICONIC-LEAD study design

Moderate-to-Severe Plaque PsO (N=684)

Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥10%
- PASI score ≥12
- Investigator's Global Assessment (IGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO



QD=once daily, ***R***=randomization.

Outcomes & Analyses

Percent improvement in PASI score through W24

- **PASI:** Assesses extent and severity (based on intensity of erythema, induration, and scaling) of PsO across 4 body regions (head, trunk, upper & lower extremities); higher scores indicate more severe disease[5]
- **Data Handling:**
  - No improvement from baseline: Pts who 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: Pts who discontinued study drug for other reasons
  - Missing data: Not imputed; handled through correlation of repeated measure in the mixed-effect model for repeated measures (MMRM)

Absolute PASI (aPASI) thresholds through W24

- **aPASI thresholds:**
  - ≤5, ≤4, ≤3, ≤2, ≤1, and 0
  - Treatment targets: ≤3 within initial 3-4 months or ≤2[1,2]
- **Data Handling:**
  - Nonresponder imputation: Pts who 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: Pts who discontinued study drug for other reasons
  - After accounting for above intercurrent events, pts with missing data were considered nonresponders

Results

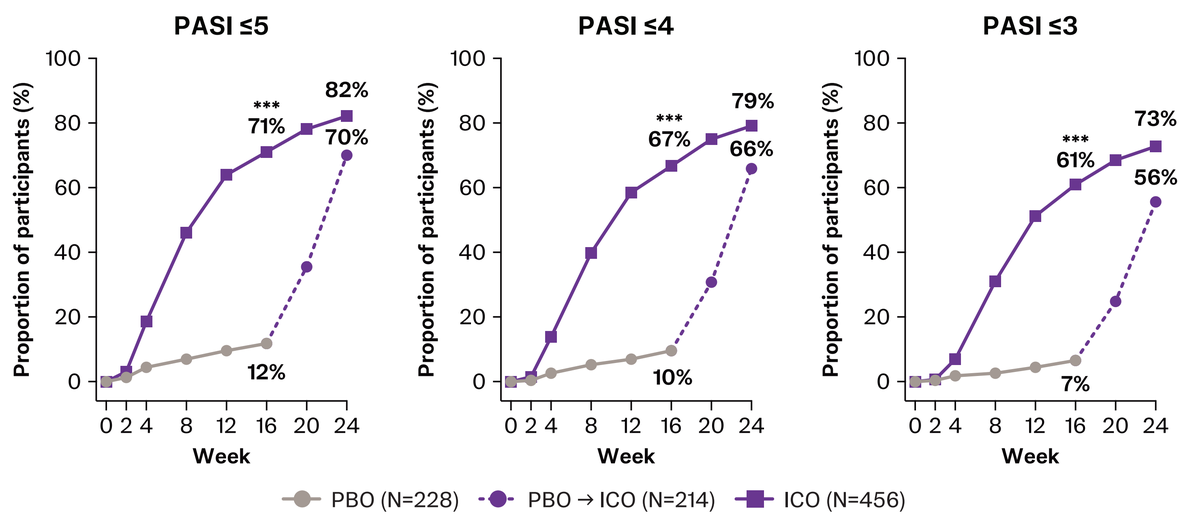
Baseline characteristics were similar between randomized treatment groups

Baseline Characteristics		ICO (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 (PUVA and UVB)	30%	29%
	Systemic therapy[b]	72%	71%
	Biologic therapy[c]	32%	37%

*Data shown are mean (SD) unless otherwise noted. [a]ICO: N=455; PBO: N=227. [b]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [c]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. **BMI**=body mass index, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **UVB**=ultraviolet B.*

ICO-treated pts achieved higher rates of aPASI thresholds of ≤5, ≤4, and ≤3 vs PBO at W16

- ICO response rates continued to increase through W24

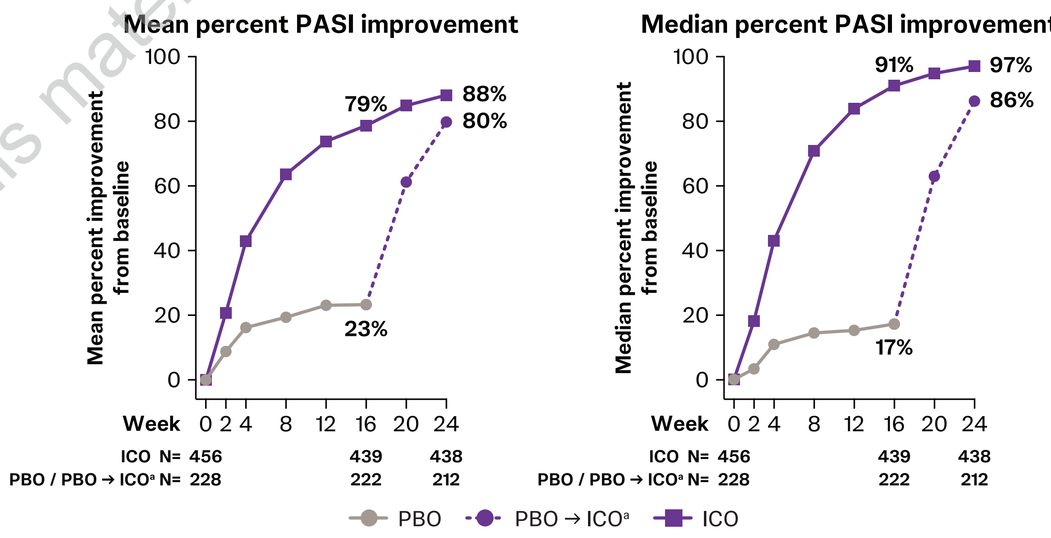


***Nominal *p*<0.001 vs PBO[a]

[a]*p-values based on Cochran-Mantel-Haenszel (CMH) chi-square test stratified by age group, baseline weight category for adults, and geographic region.*

ICO-treated pts exhibited greater mean and median percent PASI improvements vs PBO through W16

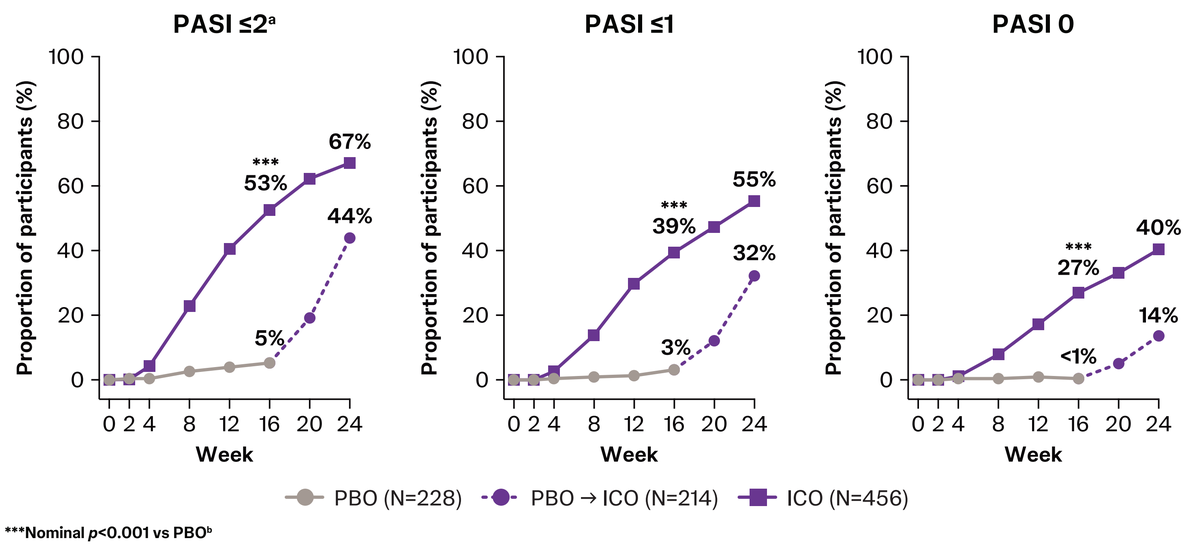
- ICO showed separation from PBO as early as W2, with increasing percent PASI improvement through W24
- ICO-treated pts achieved greater least squares (LS) mean percent PASI improvement vs PBO at W16 (80% vs 25%, respectively; nominal *p*<0.001[b])



[a]*Includes pts who transitioned from PBO to ICO at W16.* [b]*p-value based on the MMRM model with treatment group, visit, treatment group by visit interaction, age group, baseline weight, geographic region, baseline PASI total score, and baseline PASI total score by visit interaction as covariates.*

ICO-treated pts achieved higher rates of stringent aPASI thresholds (≤2, ≤1, and 0) vs PBO at W16

- ICO response rates continued to increase through W24



***Nominal *p*<0.001 vs PBO[b]

[a]*Per the British Association of Dermatologists Biologics and Immunomodulators Register, a relevant treat-to-target approach for a clinical setting is aPASI ≤2.*[1] [b]*p-values based on CMH chi-square test stratified by age group, baseline weight category for adults, and geographic region.*

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Key Takeaways

In ICONIC-LEAD, pts with moderate-to-severe plaque PsO receiving the targeted oral peptide ICO:

- **Exhibited early separation from PBO and robust high-level percent PASI improvements through W24**
- **Demonstrated higher rates of achieving aPASI thresholds, including those indicating stringent disease control, vs PBO at W16, with even higher response rates at W24**
  - ✓ **Nearly 70% of ICO-treated pts achieved a relevant treatment target of PASI ≤2 and >50% achieved PASI ≤1 at W24**

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