

Maintenance of Response With Icotrokinra, a Targeted Oral Peptide, for the Treatment of Moderate-to-Severe Plaque Psoriasis: Randomized Treatment Withdrawal in Adults (Weeks 24–52) and Continuous Treatment in Adolescents (Through Week 52) From the Phase 3, ICONIC-LEAD Trial

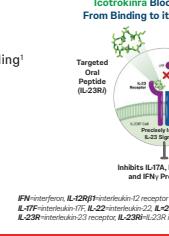


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Background

- Patients with moderate-to-severe plaque psoriasis (PsO) are limited to injectable therapies to achieve high-level efficacy with a favorable safety profile.
- Icotrokinra (ICO), a first-in-class targeted oral peptide:
 - Selectively binds the interleukin-23 receptor (IL-23R) and precisely inhibits IL-23 pathway signaling¹
 - Demonstrated significantly higher rates of skin clearance vs placebo (PBO) at Week (W)16, with increasing response rates and no safety signal through W24 in adults & adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study²



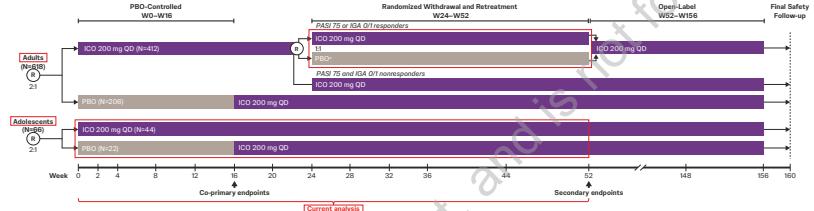
ICONIC-LEAD – Study Design

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

Key inclusion criteria

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

^aParticipants retreated with ICO upon loss of ≥50% PASI improvement observed at W24. BSA=body surface area, ICO=icotrokinra, IGA=Investigator's Global Assessment, PASI=Psoriasis Area and Severity Index, PBO=placebo, PsO=psoriasis, QD=daily, R=randomization, W=week



Objective

- Report maintenance of ICO clinical response during the randomized-withdrawal period in adults (ICO vs PBO from W24–52), longer-term ICO effects in adolescents (through W52), and safety through W52 of ICONIC-LEAD

Adult W24 ICO Responders: Psoriasis Area and Severity Index (PASI) & Investigator's Global Assessment (IGA) Responses From W24 Through W52

- Key Secondary Endpoints^b**
 - Response rates at W52^c
 - PASI 75 among PASI 75 responders at W24
 - PASI 90 among PASI 90 responders at W24
 - Time to loss of response (LOR) through W52^c
 - Loss of PASI 75 among PASI 75 responders at W24
 - Loss of PASI 90 among PASI 90 responders at W24
- Other Secondary Endpoints**
 - Response rates at W52^c
 - IGA 0/1 & ≥2-grade improvement from baseline among IGA 0/1 responders at W24
 - Time to LOR through W52^c
 - Time to loss of IGA 0/1 among IGA 0/1 responders at W24

^aAdults randomized to ICO at baseline who were PASI 75 or IGA 0/1 responders at W24. ^bMultiplicity-adjusted p-values for ICO vs PBO at/through W52. ^cParticipants considered nonresponders or to have LOR discontinued study drug due to a lack of efficacy or AE of worsening PsO; initiated a prohibited medication that could impact PsO; or met retreatment criterion for participants randomized to PBO at W24. For binary endpoints, nonresponder imputation was used for missing data (not reported for LOR). AE=adverse event; ICO=icotrokinra; IGA=Investigator's Global Assessment; LOR=loss of response; PASI=Psoriasis Area and Severity Index; PBO=placebo; PsO=psoriasis; W=week.

Adolescents: PASI & IGA Responses Through W52^c

- PASI 75
- PASI 90
- IGA 0/1 & ≥2-grade improvement from baseline

Key Takeaways

In the pivotal phase 3 ICONIC-LEAD study evaluating the targeted oral peptide ICO through 1 year in adults & adolescents with moderate-to-severe plaque PsO:

Continuous ICO demonstrated superior maintenance of skin response among adult W24 ICO responders:

- ✓ 89% and 84% maintained PASI 75 and PASI 90, respectively, at W52
- ✓ LOR vs ICO withdrawal: Not reached vs 17 weeks (PASI 75) or 10 weeks (PASI 90)

Continuous ICO demonstrated robust and durable skin clearance rates in adolescents through W52:

- ✓ PASI 90: 86%; PASI 75: 95%; IGA 0/1: 82%

ICO AE profile through W52 was consistent with that observed through W16; no ICO safety signal was identified through W52

Results

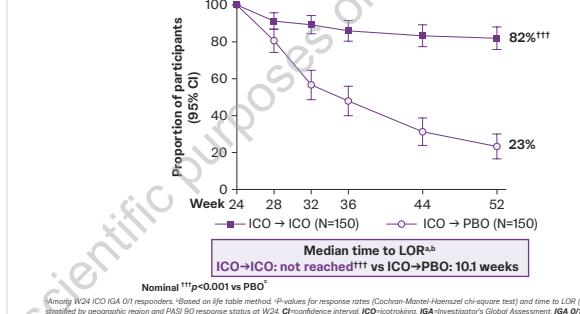
Baseline characteristics were generally comparable across re-randomized treatment groups

^aAmong 412 adults randomized to ICO at baseline, 341 (83%) were recorded as PASI 75 or IGA 0/1 responders at W24

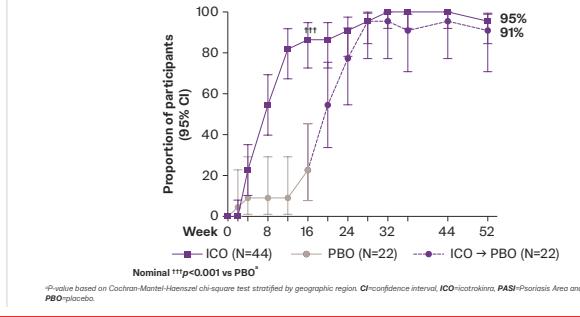
Baseline Characteristics: Adult W24 ICO Responders*		
	ICO → ICO (N=169)	ICO → PBO (N=172)
Demographics		
Age, yrs	46.5 (14.4)	44.5 (14.4)
Female	30%	38%
Race, Asian / Black / White	23% / 1% / 74%	24% / 1% / 73%
BMI, kg/m ²	29.0 (6.8)	29.7 (6.7)
Disease Characteristics		
PsO disease duration, yrs	19.2 (14.1)	18.6 (13.9)
% BSA with PsO	24.8 (14.0)	24.9 (14.7)
IGA score		
Moderate (3)	74%	78%
Severe (4)	26%	22%
PASI (0–72)	19.6 (6.7)	19.2 (7.3)
Prior PsO Treatments		
Phototherapy (PUVA or UVB)	31%	31%
Systemic therapy ^b	76%	72%
Biologic therapy ^b	35%	33%

Data shown are mean (SD), unless otherwise noted. ^aConventional biologic systemic, novel biologic systemic, 1,25-vitamin D3 and calcineurin, phototherapy, and biologics. ^bAdalimumab, dactitinab, brodalumab, ixekizumab, certolizumab pegol, efalizumab, denilumab, guselkumab, infliximab, natalizumab, secukinumab, tildrakimab, and ustekinumab. BSA=body surface area; ICO=icotrokinra; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PBO=placebo; PsO=psoriasis.

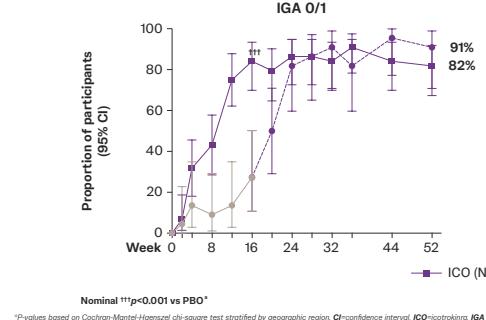
W24 ICO responders re-randomized to ICO demonstrated greater maintenance of IGA 0/1 response vs PBO at W52



Adolescents: All (100%) ICO-randomized adolescents achieved PASI 75 by W32, with response rates maintained through W52



~90% of ICO-randomized adolescents achieved clear/almost clear skin by W24, with durable response rates through W52



ICO AE profile through W52 was consistent with that observed through W16

- ICO AE profile in adolescents through W52 was consistent with that observed in the overall study population

	PBO-Controlled ^d (Adults & Adolescents)	Active Treatment (Adults & Adolescents)	ICO Responders Re-Randomized at W24 (Adults)
AEs Through W52			
Mean weeks of follow-up	15.9	15.8	
Any AE	226 (50%)	112 (49%)	
Most Common AEs			
Nasopharyngitis	31 (7%)	15 (7%)	23 (11%)
Upper respiratory tract infection	30 (7%)	16 (7%)	52 (11%)
SAE	6 (1%)	6 (3%)	4 (2%)
Serious infection	1 (1%)	0	1 (<1%)
AE Leading to Discontinuation	6 (1%)	1 (<1%)	4 (2%)
Gastrointestinal AE ^e	26 (6%)	13 (6%)	9 (4%)
Active TB	0	0	0
Malignancy ^f	2 (<1%)	0	2 (<1%)

^aAmong W24 ICO 75 and 90 responders, respectively. ^bBased on life table method. ^cp-values for response rates (Cochran-Mantel-Haenszel chi-square test) and time to LOR (log-rank test) were stratified by geographic region (and for PASI 75, also stratified by PASI 90 response status at W24). CI=confidence interval; ICO=icotrokinra; PASI=Psoriasis Area and Severity Index; PBO=placebo.

^dp-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region. CI=confidence interval; ICO=icotrokinra; IGA 0/1=IGA score 0/1 & ≥2-grade improvement from baseline. PASI=Psoriasis Area and Severity Index; PBO=placebo.

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