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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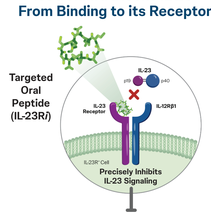
Background

- 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 signaling[1]
  - 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 study[2]

Icotrokinra Blocks IL-23 From Binding to its Receptor



IFN=interferon, ***IL-12Rβ1***=interleukin-12 receptor beta 1, ***IL-17A***=interleukin-17A, ***IL-17F***=interleukin-17F, ***IL-22***=interleukin-22, ***IL-23***=interleukin-23, ***IL-23R***=interleukin-23 receptor, ***IL-23Ri***=IL-23R inhibitor.

Objective

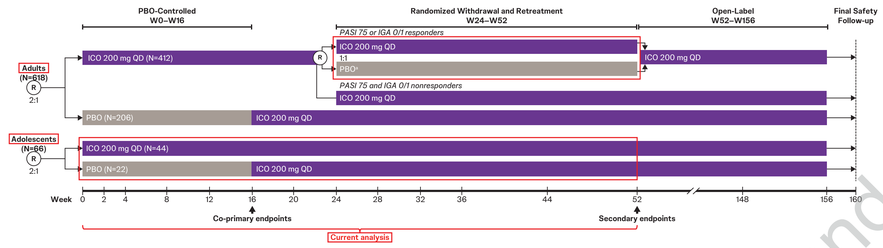
Report maintenance of ICO clinical response during the randomized-withdrawal period in adults (ICO vs PBO from W24–52), longer-term ICO effects in adolescents (through W52), and safety through W52 of ICONIC-LEAD

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



*Participants 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***=once daily, ***R***=randomization, ***W***=week.

Adult W24 ICO Responders[a]: 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

Adolescents: PASI & IGA Responses Through W52[c]

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

[a]Adults randomized to ICO at baseline who were PASI 75 or IGA 0/1 responders at W24; [b]Multiplicity-adjusted p-values for ICO vs PBO at/through W52; [c]Participants 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 imputed 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.

Results

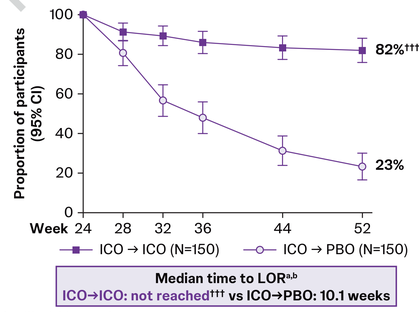
Baseline characteristics were generally comparable across re-randomized treatment groups

- *Among 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/m²	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[a]	76%	72%
Biologic therapy[b]	35%	33%

Data shown are mean (SD), unless otherwise noted. [a]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [b]Adalimumab, alefacept, bimekizumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. ***BMI***=body mass index, ***BSA***=body surface area, ***ICO***=icotrokinra, ***IGA***=Investigator's Global Assessment, ***PASI***=Psoriasis Area and Severity Index, ***PBO***=placebo, ***PsO***=psoriasis, ***PUVA***=psoralen plus ultraviolet A, ***SD***=standard deviation, ***UVB***=ultraviolet B, ***W***=week.

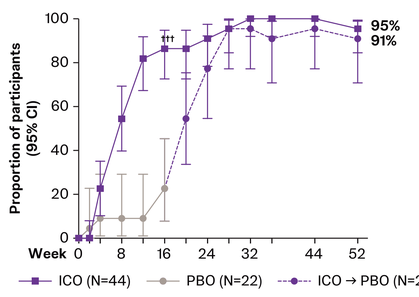
W24 ICO responders re-randomized to ICO demonstrated greater maintenance of IGA 0/1 response vs PBO at W52



Nominal †††$p<0.001$ vs PBO[c]

[a]Among W24 ICO IGA 0/1 responders. [b]Based on life table method. [c]P-values for response rates (Cochran-Mantel-Haenszel chi-square test) and time to LOR (log-rank test) were stratified by geographic region and PASI 90 response status at W24. ***CI***=confidence interval, ***ICO***=icotrokinra, ***IGA***=Investigator's Global Assessment, ***IGA 0/1***=IGA score 0/1 and ≥2-grade improvement from baseline, ***LOR***=loss of response, ***PASI***=Psoriasis Area and Severity Index, ***PBO***=placebo, ***W***=week.

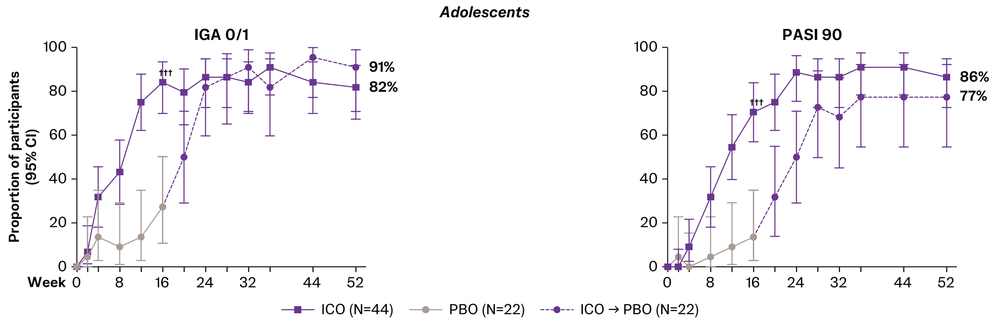
Adolescents: All (100%) ICO-randomized adolescents achieved PASI 75 by W32, with response rates maintained through W52



Nominal †††$p<0.001$ vs PBO[a]

[a]P-value based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region, ***CI***=confidence interval, ***ICO***=icotrokinra, ***PASI***=Psoriasis Area and Severity Index, ***PBO***=placebo.

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

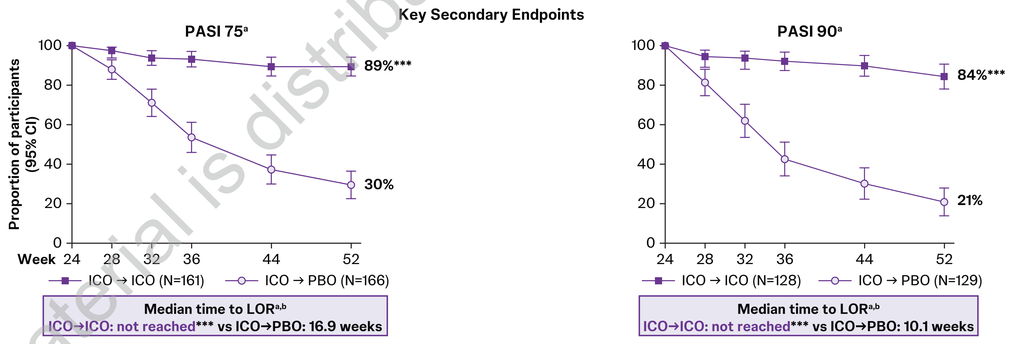


Nominal †††$p<0.001$ vs PBO[a]

[a]P-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region. ***CI***=confidence interval, ***ICO***=icotrokinra, ***IGA 0/1***=Investigator's Global Assessment score 0/1 & ≥2-grade improvement from baseline, ***PASI***=Psoriasis Area and Severity Index, ***PBO***=placebo.

W24 ICO responders re-randomized to ICO demonstrated superior maintenance of PASI response vs PBO at W52

Key Secondary Endpoints



Multiplicity-adjusted ***$p<0.001$ vs PBO[c]

[a]Among W24 ICO PASI 75 and PASI 90 responders, respectively. [b]Based on life table method. [c]P-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, ***LOR***=loss of response, ***PASI***=Psoriasis Area and Severity Index, ***PBO***=placebo, ***W***=week.

ICO adverse event (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[2] (Adults & Adolescents)		Active Treatment (Adults & Adolescents)		ICO Responders Re-Randomized at W24 (Adults)	
AEs Through W52	**ICO (W0–16; N=456)**	**PBO (W0–16; N=228)**	**ICO[a] (W16–52; N=213)**	**ICO (W0–52; N=456)**	**ICO → ICO (W24–52; N=168)**	**ICO → PBO[b] (W24–52; N=172)**
Mean Weeks of Follow-up	15.9	15.8	35.3	43.4	27.7	27.8
Any AE	226 (50%)	112 (49%)	132 (62%)	313 (69%)	92 (55%)	82 (48%)
Most Common AEs						
Nasopharyngitis	31 (7%)	15 (7%)	23 (11%)	64 (14%)	21 (12%)	20 (12%)
Upper respiratory tract infection	30 (7%)	16 (7%)	24 (11%)	52 (11%)	9 (5%)	15 (9%)
SAE	6 (1%)	6 (3%)	4 (2%)	16 (4%)	3 (2%)	5 (3%)
Serious Infection	1 (<1%)	0	1 (<1%)	1 (<1%)	0	1 (1%)
AE Leading to Discontinuation	6 (1%)	1 (<1%)	4 (2%)	10 (2%)	1 (1%)	3 (2%)
Gastrointestinal AE[c]	26 (6%)	13 (6%)	9 (4%)	51 (11%)	7 (4%)	8 (5%)
Active TB	0	0	0	0	0	0
Malignancy[d]	2 (<1%)	0	0	2 (<1%)	0	0

Safety analysis set included all randomized and treated participants. [a]Includes data after W16 for PBO-randomized participants who crossed over to receive ICO. [b]Combined withdrawal and retreatment group. [c]Based on gastrointestinal disorders SOC. [d]Included adenocarcinoma of colon and prostate cancer. ***AE***=adverse event, ***ICO***=icotrokinra, ***PBO***=placebo, ***SAE***=serious adverse event, ***SOC***=system organ class, ***TB***=tuberculosis, ***W***=week.

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**

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