Icotrokinra, a Novel Targeted Oral Peptide (IL-23R-inhibitor), in Adolescents With Moderate-to-Severe Plaque Psoriasis: Results of Subgroup Analyses From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study (ICONIC-LEAD)

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Key Takeaways

ICONIC-LEAD is the first pivotal Phase 3 trial evaluating a systemic advanced therapy for moderate-to-severe plaque PsO simultaneously in adults *and* adolescents

- **Adolescents receiving ICO achieved higher rates of *clear/almost clear* and *completely clear skin* than PBO at W16**
- **In adolescents receiving ICO, skin response rates increased through W24:**
  - ***Clear/almost clear***
    - ✓ ***IGA 0/1: 86%***
    - ✓ ***PASI 90: 89%***
  - ***Completely clear***
    - ✓ ***IGA 0: 75%***
    - ✓ ***PASI 100: 64%***
- **ICO demonstrated a favorable safety profile in adolescents through W16, consistent with the overall study population**
- **No safety signal was identified through W24**

Results from adolescent participants with moderate-to-severe plaque PsO complement those from the overall ICONIC-LEAD study population through W24[5]

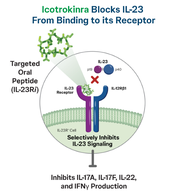
Background

Pediatric plaque psoriasis (PsO)
Approximately one-third of patients with plaque PsO report onset before adulthood; however, few advanced treatment options are available[1]

Icotrokinra
Patients with moderate-to-severe plaque PsO are generally limited to injectable therapies to achieve high-level efficacy with a favorable safety profile

Icotrokinra (ICO) is a first-in-class, targeted oral peptide that:

- Selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 signaling[2]
- Demonstrated significant skin clearance and no safety signals through 1 year in Phase 2 PsO studies[3,4]
- Demonstrated significantly higher rates of almost clear and/or completely clear skin vs placebo (PBO) at Week (W)16 and no safety signals through W24 among all participants with moderate-to-severe plaque PsO in ICONIC-LEAD, the first pivotal Phase 3 trial evaluating a systemic advanced therapy in adults and adolescents[5]



IFN=interferon, IL=interleukin, IL-23R=interleukin-23 receptor, IL-23Ri=interleukin-23 receptor inhibitor.

Objective

Key clinical outcomes and adverse events (AEs) from the ICONIC-LEAD adolescent subgroup through W24 are reported

ICONIC-LEAD – Study Design & Adolescent Subgroup

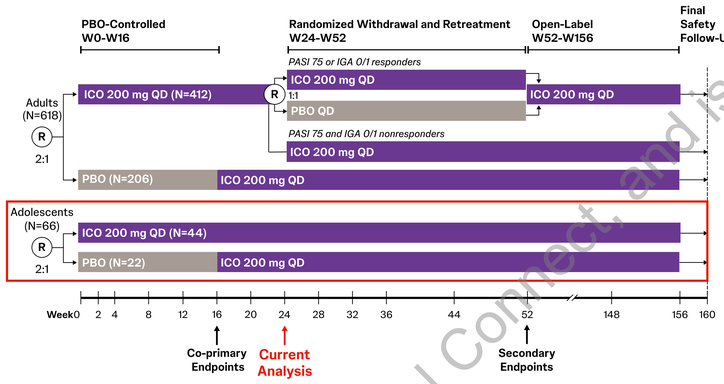
Moderate-to-severe plaque PsO (N=684)

Key inclusion criteria:

- ≥12 years, including
  - Adults (≥18 years)
  - Adolescents (12-<18 years)
- Plaque PsO ≥26 weeks
- BSA ≥10%, PASI ≥12, IGA ≥3
- Candidate for photo-therapy or systemic PsO treatment

Adolescent-specific inclusion criteria:

- Body weight ≥40 kg[a]



*[a]Weight limit was set to ensure similar exposures between adults and adolescents. **BSA**=body surface area, **ICO**=icotrokinra, **IGA**=Investigator Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **QD**=once daily, **R**=randomized, **W**=week.*

Methods

Endpoints & statistical considerations

Endpoints in adolescents

- Overall ICONIC-LEAD co-primary endpoints at W16
  - Investigator Global Assessment (IGA) 0/1 response (IGA score of cleared [0] or minimal [1] and ≥2-grade improvement from baseline)
  - Psoriasis Area and Severity Index (PASI) 90 response (≥90% improvement from baseline in total PASI score)
- Select key secondary endpoints assessing complete skin clearance at W16
  - IGA 0 response
  - PASI 100 response
- Assessment of clinical response and AEs continued through W24

Statistical considerations

- Adolescents were analyzed as a subgroup of the ICONIC-LEAD study
- Nominal p-values for ICO vs PBO at W16 were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region (the Americas, the European Union, Asia-Pacific; 2-sided α=0.05)
- Participants with the following intercurrent events (ICE) were considered as nonresponders:
  - Discontinued study drug due to lack of efficacy or AE of worsening of PsO (ICE 1)
  - Initiated prohibited medication that could impact PsO (ICE 2)
- Observed data were used for participants with an ICE of discontinuing study agent due to other reasons
- After accounting for these ICE, NRI was applied to participants with missing data

Results

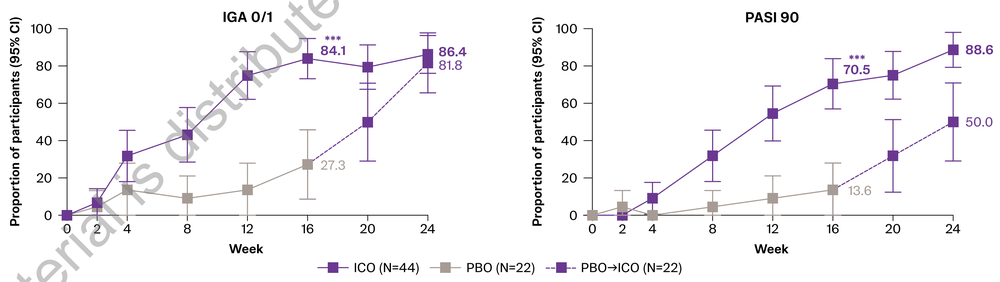
Adolescent baseline characteristics were generally balanced across groups

Baseline characteristics of adolescents	ICO 200 mg QD (N=44)	PBO (N=22)
Demographics		
Age, years	15.0 (1.8)	15.0 (1.5)
Female	52%	64%
Race, Asian/Black/White	23/4/70%	23/0/77%
BMI, kg/m^2	26.0 (7.1)	24.4 (7.9)
Disease characteristics		
PsO disease duration, years	4.9 (4.0)	5.8 (3.4)
% BSA with PsO	26.1 (15.6)	27.1 (14.0)
IGA score		
Moderate (3)	70%	82%
Severe (4)	30%	18%
PASI (0–72)	19.8 (8.2)	18.6 (4.0)
Prior treatment for PsO		
Systemic therapy[a]	52%	50%
Biologic therapy[b]	14%	41%
Phototherapy (PUVA or UVB)	23%	14%

*Data shown are mean (SD) unless specified otherwise. [a]Includes conventional nonbiologic, novel nonbiologic, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [b]Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, and certolizumab pegol. **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, **QD**=once daily, **UVB**=ultraviolet B, **SD**=standard deviation.*

ICO demonstrated high rates of *clear/almost clear skin* in adolescents at W16 and W24

Clear/Almost Clear Skin Over Time in Adolescents

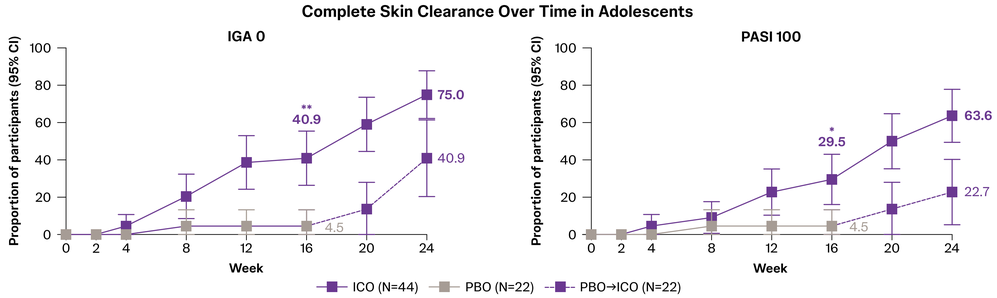


***nominal p<0.001 vs PBO; IGA 0/1 at W16: Δ 56.2% (33.2%, 74.1%); PASI 90 at W16: Δ 56.3% (32.5%, 73.0%).

*Note: 95% CIs are based on the normal assumption without adjustment (Wald Method). PBO→ICO includes PBO participants who crossed over to receive ICO at W16 through W24. Participants with ICE 1-2 or missing data were imputed as nonresponders through W24. P-value derived from Cochran-Mantel-Haenszel chi-square test stratified by geographic region. **CI**=confidence interval, **ICE**=intercurrent event, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.*

ICO demonstrated high rates of *completely clear skin* in adolescents at W16 and W24

Complete Skin Clearance Over Time in Adolescents



**nominal p<0.01 vs PBO; IGA 0 at W16: Δ 35.7% (14.6%, 51.9%); *nominal p<0.05 vs PBO; PASI 100 at W16: Δ 24.4% (4.9%, 40.6%).

*Note: 95% CIs are based on the normal assumption without adjustment (Wald Method). PBO→ICO includes PBO participants who crossed over to receive ICO at W16 through W24. Participants with ICE 1-2 or missing data were imputed as nonresponders through W24. P-value derived from Cochran-Mantel-Haenszel chi-square test stratified by geographic region. **CI**=confidence interval, **ICE**=intercurrent event, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.*

ICO demonstrated a *favorable safety profile* through W16 in adolescents, consistent with the overall study population

	Adolescents		Overall Study Population	
AEs through W16	ICO 200 mg QD (N=44)	PBO (N=22)	ICO 200 mg QD (N=456)	PBO (N=228)
Mean weeks of follow-up	16.2	16.2	15.9	15.8
Any AE, n (%)	22 (50)	16 (73)	225 (49)	112 (49)
Infection, n (%)	14 (32)	6 (27)	107 (24)	51 (22)
Upper respiratory tract infection	6 (14)	1 (4)	30 (7)	16 (7)
Nasopharyngitis	5 (11)	3 (14)	31 (7)	15 (7)
SAE, n (%)	2 (4)[a,b]	10	6 (1)	6 (3)

*[a]17-year-old female with a medical history of obesity and a gastric sleeve procedure leading to rapid weight loss before entering the study. CT and ultrasound showed pancreatitis due to choledocholithiasis. Cholecystectomy was performed and she was discharged in good condition. Treatment was interrupted but resumed after resolution and she continues in the study. [b]17-year-old female with medical history of joint pain was admitted to the hospital at W4 of the study for further diagnostic evaluation of joint pain. No imaging studies were completed. Treatment was continued without interruption. She was discharged the next day in good condition. No diagnosis was confirmed. **AE**=adverse event, **ICE**=intercurrent event, **ICO**=icotrokinra, **PBO**=placebo, **QD**=once daily, **SAE**=serious AE, **W**=week.*

- In adolescents through W24 of ICO:
  - Most common AEs were consistent with those observed through W16 (upper respiratory tract infection, nasopharyngitis)
  - No active TB, malignancy, or death
  - No safety signal emerged
- The proportions of adolescents with clinical laboratory abnormalities were similar between ICO and PBO groups through W16 and remained low through W24 of ICO

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