Consistency of Skin Clearance With the Targeted Oral Peptide Icotrokinra: Results From a Large Pooled Cohort of Phase 3 Study Participants With Moderate-to-Severe Plaque Psoriasis

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Key Takeaways

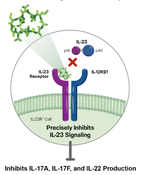
- **In a large pooled cohort of adults and adolescents with moderate-to-severe plaque PsO, the targeted oral peptide ICO demonstrated:**
  - **Robust rates of skin clearance at W16**
  - **Consistent treatment effects regardless of:**
    - **Sex, age, weight, and body mass index**
    - **PsO disease severity**
    - **Prior PsO treatment**
  - **An AE profile similar to PBO through W16**
- **Findings suggest that once-daily oral ICO provides high-level skin improvements across broad groups of participants with moderate-to-severe PsO**

Background

Icotrokinra (ICO) for Plaque Psoriasis (PsO)
First and only targeted oral peptide that precisely blocks the interleukin-23 (IL-23) receptor and inhibits IL-23 pathway signaling[1]

Evaluated for the treatment of moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2 studies[2,3]

- Co-primary endpoints of each study were met, with ICO demonstrating significantly higher rates of clear/almost clear skin versus placebo (PBO) at Week (W) 16



*IL=interleukin, **IL-12Rβ1**=interleukin-12 receptor beta 1, **IL-23R**=interleukin-23 receptor–positive.*

Objective

Evaluate the consistency of ICO versus PBO skin clearance response at W16 across baseline subgroups of high clinical interest in a large pooled cohort of phase 3 study participants

Pooled ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2: ICO Versus PBO Through W16 by Baseline Subgroups

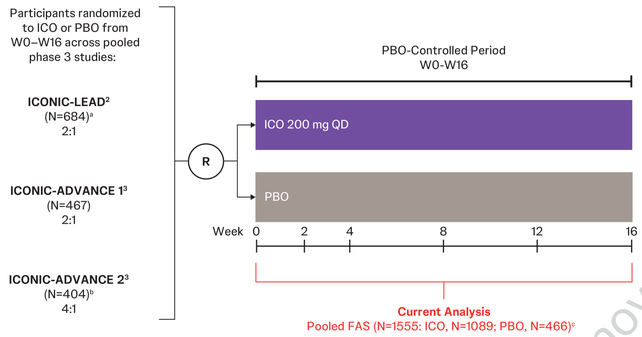
Moderate-to-Severe Plaque PsO (N=1555)

Key inclusion criteria

- ≥12 yrs ICONIC-LEAD
- ≥18 yrs ICONIC-ADVANCE 1 & 2
- Plaque PsO ≥26 weeks
- BSA ≥10%, PASI score ≥12, IGA score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO

Co-primary endpoints

- IGA score of 0/1 and ≥2-grade improvement from baseline (IGA 0/1) versus PBO at W16
- ≥90% reduction in PASI score from baseline (PASI 90) versus PBO at W16



[a]Adolescents, n=66. [b]ICONIC-ADVANCE 2 enrolled 404 participants in the ICO and PBO groups, of whom 401 were evaluable for efficacy. [c]Includes participants who were randomized to ICO or PBO from the pooled phase 3 ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2 studies. Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).
***BSA**=body surface area, **FAS**=full analysis set, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **QD**=once daily, **R**=randomization, **W**=week.*

Outcomes & Analyses

W16 IGA 0/1 Response[a,c]

- Proportion difference (95% CI) between ICO and PBO IGA 0/1 response
- Subgroups of high clinical interest:
  - Demographic characteristics (sex, age, body weight, and body mass index)
  - PsO disease characteristics (PASI and IGA)
  - Prior PsO treatment (biologics and systemics)

W16 Percent PASI Improvement[b,d]

- LS mean percent improvement from baseline in PASI score
- Subgroups of interest:
  - Body weight quartiles
  - Body mass index categories

[a]Nonresponder imputation / [b]No improvement from baseline assigned after participants discontinued the study drug due to a lack of efficacy or an AE of worsening PsO, or initiated prohibited medication that could impact PsO. Observed data were used for participants who discontinued the study drug for other reasons. [c]After accounting for the intercurrent events, participants with missing data were considered nonresponders. [d]The remaining missing data were not imputed and were accounted for through the MMRM model.
***AE**=adverse event, **CI**=confidence interval, **ICO**=icotrokinra, **IGA**=investigator's global assessment, **LS**=least square, **MMRM**=mixed-effect model for repeated measures, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsA**=psoriatic arthritis, **PsO**=psoriasis, **W**=week.*

Results

ICO consistently demonstrated higher IGA 0/1 response rates versus PBO at W16 across subgroups defined by sex, age, weight, body mass index, baseline disease severity, and prior biologic/systemic treatment

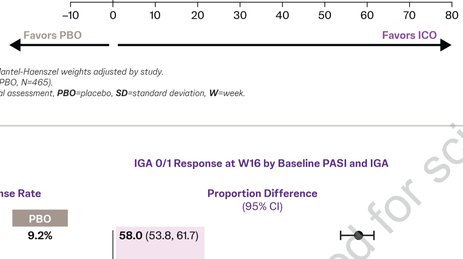
Baseline Demographic Characteristics in the Pooled Phase 3 Cohort

	ICO	PBO	ICO	PBO
			Response Rate	
Pooled FAS	N=1089	N=466	**67.6%**	**9.2%**
Sex				
Male	732 (67%)	316 (68%)	**66.0%**	**7.9%**
Female	357 (33%)	150 (32%)	**71.0%**	**12.0%**
Age, years	44.8 (14.9)	45.4 (15.1)		
≥12 to <18	44 (4%)	22 (5%)	**84.1%**	**27.3%**
≥18 to <45	505 (46%)	197 (42%)	**68.3%**	**9.6%**
≥45 to <65	435 (40%)	194 (42%)	**63.7%**	**6.7%**
≥65	105 (10%)	53 (11%)	**73.3%**	**9.6%**

Data shown are mean (SD) or n (%).

Participant demographic characteristics were balanced across treatment groups

IGA 0/1 Response at W16 by Sex and Age at Baseline



95% CI for difference in proportion is based on the Miettinen-Nurminen method using Mantel-Haenszel weights adjusted by study.
Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).
***CI**=confidence interval, **FAS**=full analysis set, **ICO**=icotrokinra, **IGA**=investigator's global assessment, **PBO**=placebo, **SD**=standard deviation, **W**=week.*

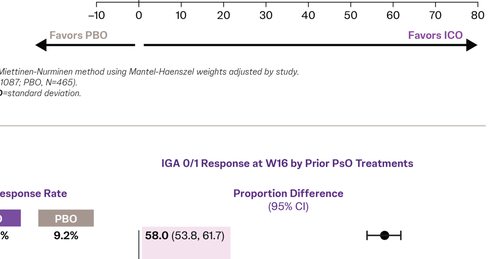
Baseline Demographic Characteristics in the Pooled Phase 3 Cohort

	ICO	PBO	ICO	PBO
			Response Rate	
Pooled FAS	N=1089	N=466	**67.6%**	**9.2%**
Weight, kg	87.1 (21.0)	87.1 (23.2)		
≤90	649 (60%)	276 (59%)	**71.4%**	**10.9%**
>90	440 (40%)	190 (41%)	**62.0%**	**6.9%**
Body mass index,[a] kg/m²	29.4 (6.6)	29.4 (7.2)		
Normal (<25)	276 (25%)	112 (24%)	**76.7%**	**17.0%**
Overweight (≥25 to <30)	377 (35%)	166 (36%)	**69.2%**	**8.4%**
Obese (≥30)	435 (40%)	187 (40%)	**60.6%**	**5.4%**

Data shown are mean (SD) or n (%).

Body size categories were balanced across treatment groups

IGA 0/1 Response at W16 by Baseline Weight and Body Mass Index



[a]ICO, N=1088; PBO, N=465. 95% CI for difference in proportion is based on the Miettinen-Nurminen method using Mantel-Haenszel weights adjusted by study.
Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).
***CI**=confidence interval, **FAS**=full analysis set, **ICO**=icotrokinra, **PBO**=placebo, **SD**=standard deviation.*

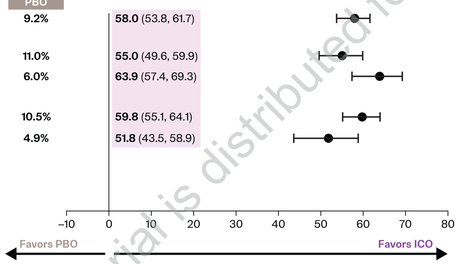
Baseline Disease Severity in the Pooled Phase 3 Cohort

	ICO	PBO	ICO	PBO
			Response Rate	
Pooled FAS	N=1089	N=466	**67.6%**	**9.2%**
PASI score (0-72)	19.8 (7.0)	20.1 (7.5)		
<20	699 (64%)	300 (64%)	**66.6%**	**11.0%**
≥20	390 (36%)	166 (36%)	**69.5%**	**6.0%**
IGA score (0-4)				
3 (moderate)	844 (78%)	363 (78%)	**70.9%**	**10.5%**
4 (severe)	245 (22%)	103 (22%)	**56.3%**	**4.9%**

Data shown are mean (SD) or n (%).

Disease characteristics were balanced across treatment groups
- Mean PsO duration: 17–18 years
- Mean PsO BSA: 26%

IGA 0/1 Response at W16 by Baseline PASI and IGA



95% CI for difference in proportion is based on the Miettinen-Nurminen method using Mantel-Haenszel weights adjusted by study.
Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).
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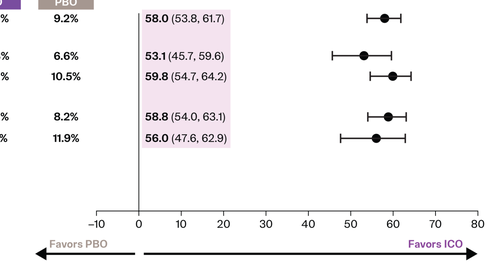
Prior PsO Treatments at Baseline in the Pooled Phase 3 Cohort

	ICO	PBO	ICO	PBO
			Response Rate	
Pooled FAS	N=1089	N=466	**67.6%**	**9.2%**
Biologics ever used				
Yes	312 (29%)	153 (33%)	**60.3%**	**6.6%**
No	777 (71%)	313 (67%)	**70.5%**	**10.5%**
Systemics ever used				
Yes	788 (72%)	331 (71%)	**67.8%**	**8.2%**
No	301 (28%)	135 (29%)	**67.1%**	**11.9%**

Data shown are n (%).

PsO treatment history was similar between treatment groups
- 32% had previous phototherapy (PUVA or UVB)

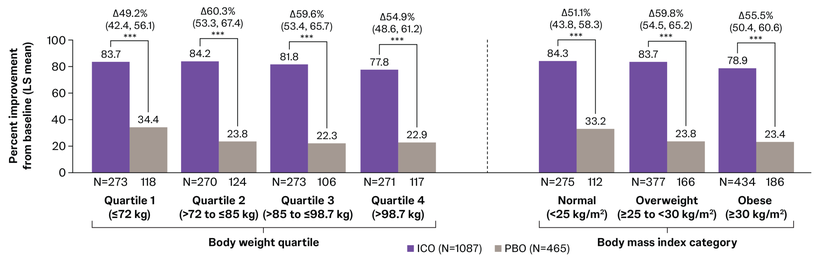
IGA 0/1 Response at W16 by Prior PsO Treatments



95% CI for difference in proportion is based on the Miettinen-Nurminen method using Mantel-Haenszel weights adjusted by study. Biologics: adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. Systemics: conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogs, phototherapy, and biologics. Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).
***CI**=confidence interval, **FAS**=full analysis set, **ICO**=icotrokinra, **IGA**=investigator's global assessment, **PBO**=placebo, **PsO**=psoriasis, **PUVA**=psoralen plus ultraviolet A, **UVB**=ultraviolet B, **W**=week.*

ICO consistently demonstrated greater mean percent PASI improvements versus PBO at W16 regardless of weight and body mass index

- In the overall pooled population, ICO provided substantially greater LS mean percent PASI improvement versus PBO at W16 (81.9% vs 25.8%, respectively; LS mean difference: 56.2% [95% CI: 52.8, 59.5]; nominal P<0.001)



****Nominal P<0.001 versus PBO. LS means, LS mean differences, and p-value were based on the MMRM model with treatment group, visit, study, baseline PASI total score, and treatment group by visit interaction as covariates. Participants with missing baseline body weight or body mass index were not included in the analysis. Among participants in the pooled FAS, 1552 were evaluable for efficacy (ICO, N=1087; PBO, N=465).* ***FAS**=full analysis set, **ICO**=icotrokinra, **LS**=least square, **MMRM**=mixed-effect model for repeated measures, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.*

In this large pooled cohort, the ICO AE profile was similar to PBO through W16

Pooled safety through W16,[a] n (%)	ICO (N=1088)	PBO (N=465)
Mean weeks of follow-up, n	15.9	15.6
Any AE	531 (49%)	249 (54%)
Most common AEs (≥5%)		
Nasopharyngitis	68 (6%)	28 (6%)
Upper respiratory tract infection	53 (5%)	24 (5%)
Serious AEs	20 (2%)	10 (2%)
AEs leading to discontinuation	20 (2%)	13 (3%)
Infections	252 (23%)	125 (27%)
Serious infections	2 (<1%)	1 (<1%)
Gastrointestinal AEs	71 (7%)	27 (6%)
Malignancy	5 (<1%)	1 (<1%)

[a]Safety analysis set included all randomized and treated participants. ***AE**=adverse effects, **ICO**=icotrokinra, **PBO**=placebo, **W**=week.*

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