LB1142

Phase 3 Results From an Innovative Trial Design of Treating Plaque Psoriasis Involving Difficult-to-Treat, High-Impact Sites With Icotrokinra, a Targeted Oral Peptide That Selectively Inhibits the IL-23–Receptor

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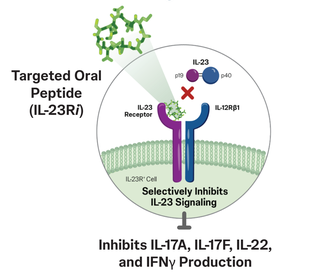
Background

Icotrokinra for plaque psoriasis

- Patients with moderate-to-severe plaque psoriasis (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 pathway signaling[1]
  - Demonstrated significant skin clearance and no safety signals through 1 year in phase 2 PsO studies[2,3] and through Week (W)24 in adults & adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study[4]

Icotrokinra Blocks IL-23 From Binding to its Receptor



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

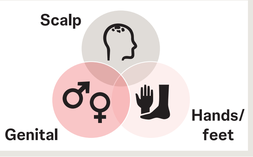
*IFN=interferon; **IL-12Rβ1**=interleukin-12 receptor beta 1; **IL-23R**=interleukin-23 receptor; **IL-23Ri**=interleukin-23 receptor inhibitor.*

Objectives

The pivotal, phase 3 ICONIC-TOTAL study evaluated ICO in adults & adolescents with plaque PsO involving difficult-to-treat, high-impact sites, by employing a novel basket-like design; key clinical/patient-reported outcomes (PROs) and safety-related findings are reported through W16

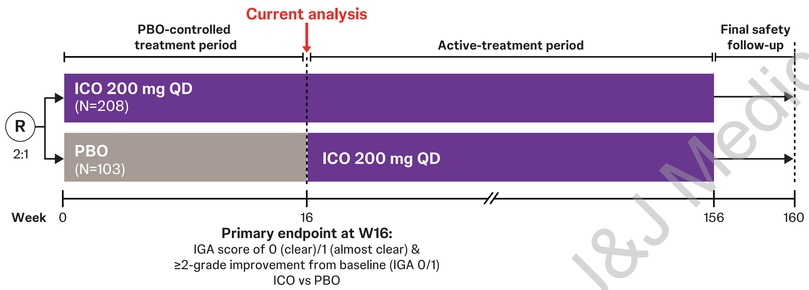
ICONIC-TOTAL: a novel basket-like design

Adults & adolescents with plaque PsO involving high-impact sites evaluated using a basket-like study design (N=311)



Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥1% and Investigator's Global Assessment (IGA) score ≥2
- At least moderate high-impact PsO involving ≥1 site:
  - **Scalp PsO:** scalp-specific IGA (ss-IGA) score ≥3
  - **Genital PsO:** static Physician's Global Assessment of Genitalia (sPGA-G) score ≥3
  - **Hand/foot PsO:** Physician's Global Assessment of hands and feet (hf-PGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical



*Participants (pts) with the following intercurrent events were considered as nonresponders: discontinued study drug due to a lack of efficacy or AE of worsening PsO or initiated prohibited medication that could impact PsO. After accounting for these intercurrent events, nonresponder imputation was applied to pts with missing data. **AE**=adverse event; **PBO**=placebo; **QD**=once daily; **R**=randomization.*

Key Takeaways

- **In ICONIC-TOTAL, a pivotal phase 3 study evaluating ICO in a diverse cohort of pts with plaque PsO and difficult-to-treat, high-impact site involvement:**
  - ✓ **ICO demonstrated significantly higher rates of clear/almost clear skin, including in the scalp and genital areas, than PBO at W16**
  - ✓ **ICO-treated pts achieved significantly higher PRO response rates, including meaningful improvements in the scalp and genital areas, vs PBO at W16**
  - ✓ **Rates of AEs were generally similar in the ICO and PBO groups; no safety signal was identified through W16**
- **ICONIC-TOTAL results complement those of the ongoing phase 3 ICONIC-LEAD study evaluating ICO in adults & adolescents with moderate-to-severe plaque PsO[4]**

Results

Baseline characteristics were generally similar between groups

- Overall, 5% of pts (ICO: 4%; PBO: 9%) discontinued treatment through W16[d]

Baseline Characteristics	ICO 200 mg QD (N=208)	PBO (N=103)
Demographics		
Age, years	45.3 (14.6)	43.5 (13.8)
Male	66%	61%
White	77%	80%
BMI, kg/m²	29.0 (6.6)[a]	29.4 (8.1)[a]
Disease Characteristics		
PsO disease duration, years	16.8 (13.3)	15.2 (10.5)
% BSA with PsO	16.6 (13.5)	14.8 (11.7)
<10%	36%	37%
≥10%	64%	63%
IGA score		
Moderate (3)	74%	71%
Severe (4)	22%	21%
PASI (0-72)	14.6 (7.6)	14.0 (7.0)
Prior Treatment for PsO		
Phototherapy (PUVA and UVB)	43%	31%
Systemic therapy[b]	73%	73%
Biologic therapy[c]	34%	31%

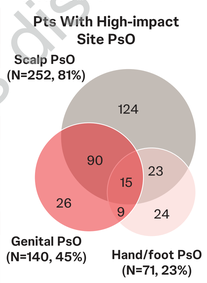
*Data shown are mean (SD), unless otherwise indicated. [a]ICO: N=203; PBO: N=101. [b]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [c]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. [d]Among the pts who discontinued treatment through W16 (ICO: n=8 [4%]; PBO: n=9 [9%]), the most common reasons for discontinuation were lack of efficacy and AEs in the ICO group (n=3 [1%] for each) and lack of efficacy in the PBO group (n=5 [5%]). **BMI**=body mass index; **PASI**=Psoriasis Area and Severity Index; **PUVA**=psoralen plus ultraviolet A; **SD**=standard deviation; **UVB**=ultraviolet B.*

Scalp and genital PsO severity at baseline was generally similar between groups

- Among the limited subset of pts with hf-PGA score ≥3, a higher proportion in the ICO group had severe involvement vs PBO

High-impact Site PsO Severity[a]	ICO 200 mg QD (N=208)	PBO (N=103)
ss-IGA score ≥3	167 (80%)	85 (83%)
Moderate (3)	80%	75%
Severe (4)	20%	25%
sPGA-G score ≥3	98 (47%)	42 (41%)
Moderate (3)	77%	69%
Severe (4)	22%	29%
Very severe (5)	1%	2%
hf-PGA score ≥3	48 (23%)	23 (22%)
Moderate (3)	65%	83%
Severe (4)	35%	17%

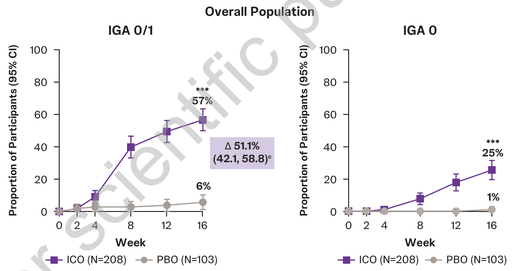
- 44% of pts had >1 high-impact site involved



Data shown are n (%), unless otherwise indicated. [a]PsO involving high-impact sites was not mutually exclusive.

ICO demonstrated significantly higher rates of IGA 0/1 vs PBO at W16 (primary endpoint)

- Significantly higher proportions of ICO-treated pts reported meaningful improvement in itch (CMI PSSD Itch,[a,b] 60% vs 14%; *P*<0.001) and symptom resolution at W16 (PSSD Symptom 0,[a,b] 16% vs 3%; *P*<0.01)

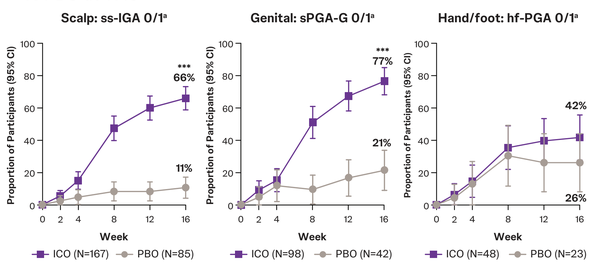


***Multiplicity-adjusted *P*<0.001 vs PBO[b]

*[a]Among pts with a baseline PSSD Itch score ≥4 or PSSD Symptom score >0. [b]P values were based on Cochran-Mantel-Haenszel chi-square test stratified by high-impact site involvement and BSA category, if applicable. [c]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for high-impact site involvement and BSA category using Mantel-Haenszel weights. **CI**=confidence interval; **CMI**=clinically meaningful improvement (≥4-point improvement from baseline); **PSSD**=Psoriasis Symptom and Sign Diary.*

ICO demonstrated significantly higher rates of clear/ almost clear scalp and genital PsO vs PBO

- A numerically greater proportion of ICO-treated pts achieved hf-PGA 0/1 vs PBO at W16

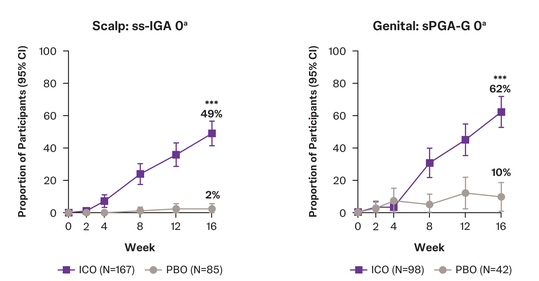


***Multiplicity-adjusted *P*<0.001 vs PBO[b]

[a]Among pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score ≥3. [b]P values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA category.

ICO demonstrated higher rates of completely clear scalp and genital PsO vs PBO

- A numerically greater proportion of ICO-treated pts achieved hf-PGA 0[a] vs PBO at W16 (25% vs 13%)

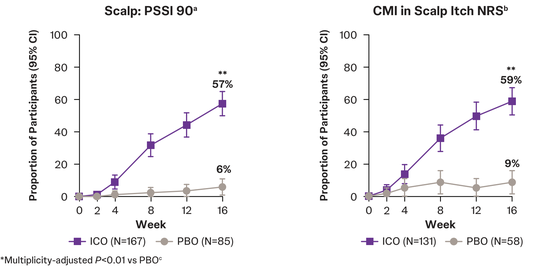


***Nominal *P*<0.001 vs PBO[b]

[a]Among pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score ≥3. [b]P values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA category.

ICO demonstrated significantly higher rates of scalp clearance and meaningful improvement in scalp itch vs PBO

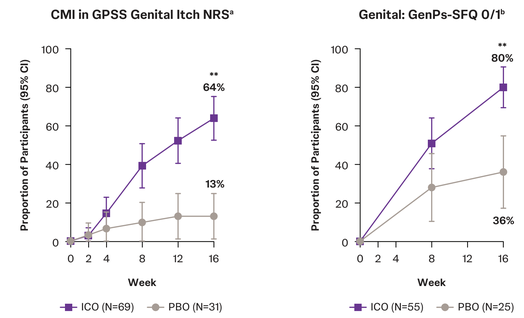
- ICO demonstrated early separation from PBO



**Multiplicity-adjusted *P*<0.01 vs PBO[c]

*[a]Among pts with a baseline ss-IGA score ≥3. [b]Among pts with a baseline Scalp Itch NRS score ≥4 and a ss-IGA score ≥3. [c]P values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and BSA category. **CMI**=clinically meaningful improvement (≥4-point improvement from baseline); **NRS**=numeric rating scale; **PSSI**=Psoriasis Scalp Severity Index; **PSSI 90**=reduction from baseline of ≥90% in the PSSI score.*

ICO significantly improved pt-reported genital PsO itch & impact of PsO on sexual activity vs PBO



**Multiplicity-adjusted *P*<0.01 vs PBO[c]

*[a]Among pts with a baseline GPSS Genital Itch NRS score (Item 1) ≥4 and a sPGA-G score ≥3. [b]Among pts with a baseline GenPs-SFQ score (Item 2) ≥2 and a sPGA-G score ≥3. [c]P values were based on Cochran-Mantel-Haenszel chi-square test stratified by BSA category. **CMI**=clinically meaningful improvement (≥4-point improvement from baseline); **GenPs-SFQ**=Genital Psoriasis Sexual Frequency Questionnaire; **GPSS**=Genital Psoriasis Symptoms Score.*

Adverse event rates were generally similar between groups through W16

	ICO 200 mg QD (N=208)	PBO (N=103)
Safety through W16		
Mean weeks of follow-up	16.0	15.7
Any AE	104 (50%)	43 (42%)
Most common AEs (≥5%)		
Nasopharyngitis	26 (12%)	11 (11%)
Upper respiratory tract infection	9 (4%)	5 (5%)
Headache	6 (3%)	6 (6%)
SAE[a]	1 (<1%)	2 (2%)
Infection	59 (28%)	22 (21%)
Serious infection	0	1 (1%)
AE leading to discontinuation[b]	4 (2%)	3 (3%)
Gastrointestinal AEs	15 (7%)	8 (8%)
Active TB	0	0
Malignancy[c]	1 (<1%)	0

*[a]SAEs through W16 included COVID-19 pneumonia, sepsis, sciatica, and acute respiratory failure in the PBO group; and hepatitis in the ICO group. [b]AEs leading to discontinuation through W16 included COVID-19 pneumonia, psoriatic arthropathy, and psoriasis in the PBO group; and vision blurred, visual field defect, laryngitis fungal, malignant melanoma in situ, and headache in the ICO group. [c]Malignancy reported in the ICO group was malignant melanoma in situ in a pt with a recent personal history of melanoma (in 2021). **COVID-19**=coronavirus disease 2019; **SAE**=serious adverse event; **TB**=tuberculosis.*

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