Treatment of Plaque Psoriasis Involving High-impact Sites With Icotrokinra, a Targeted Oral Peptide: Pooled Analyses of 4 Phase 3 Placebo-controlled Trials

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Key Takeaways

- **In large pooled phase 3 cohorts of adults and adolescents with at least moderate high-impact site PsO and/or nail PsO, the targeted oral peptide ICO demonstrated:**
  - **High rates of scalp, genital, and hand/foot PsO clearance at W24**
    - **72–84% achieved clear/almost clear high-impact site PsO**
    - **58–73% achieved completely clear high-impact site PsO**
  - **Substantial mean mNAPSI improvement (50%) at W24**
- **Consistent with findings from each study, the ICO AE profile was similar to PBO through W16[4-6]**

Background

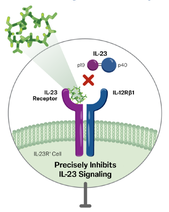
Plaque psoriasis (PsO) on high-impact sites (e.g., scalp, genitals, hands/feet, nails) can be difficult-to-treat and negatively impact patients' quality of life[1]

Patients with high-impact site PsO are candidates for systemic therapy, regardless of their body surface area (BSA) affected, per the International Psoriasis Council consensus statement[2]

Icotrokinra (ICO) is the first and only targeted oral peptide:

- Precisely blocks the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[3]
- Evaluated for the treatment of moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2 studies, and for plaque PsO involving high-impact sites in the phase 3 ICONIC-TOTAL study; primary/co-primary endpoints of each study were met, with no safety signals identified[4-6]
  - In adults and adolescents with high-impact site PsO involvement, ICO demonstrated:
    - Significantly higher scalp and genital PsO clearance rates vs placebo (PBO) at Week (W)16 (ICONIC-TOTAL)[6]
    - Higher rates of scalp, genital, and hand/foot PsO clearance and substantially improved nail PsO vs PBO at W16 (ICONIC-LEAD)[7]

Icotrokinra Blocks IL-23 From Binding to its Receptor



IL-12Rβ1=interleukin-12 receptor beta 1.

Objective

Evaluate ICO effects in pooled cohorts of participants (pts) with PsO involving high-impact sites, including the scalp, genitals, hands/feet, and/or nails, across 4 phase 3 studies

Methods

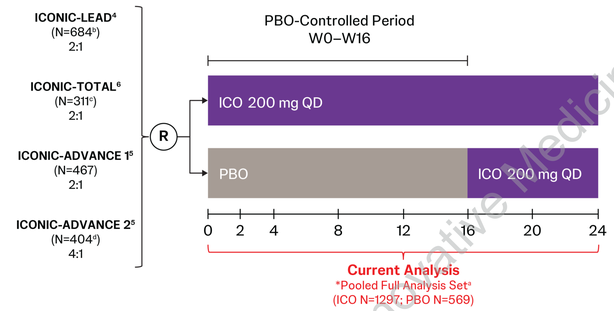
Pooled ICONIC-LEAD, -TOTAL, -ADVANCE 1 & 2: ICO vs PBO Through W16

Moderate-to-Severe or High-Impact Site Plaque PsO (N=1866*)

Key inclusion criteria

- ≥12 yrs ICONIC-LEAD & -TOTAL
- ≥18 yrs ICONIC-ADVANCE 1 & 2
- Plaque PsO ≥26 weeks
- ICONIC-LEAD, -ADVANCE 1 & 2:
  - BSA ≥10%; PASI score ≥12; IGA score ≥3
  - Candidate for phototherapy or systemic treatment for plaque PsO
- ICONIC-TOTAL:
  - BSA ≥1% and IGA score ≥2
  - At least moderate high-impact PsO involving ≥1 site: ss-IGA score ≥3; sPGA-G score ≥3; hf-PGA score ≥3
  - Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical

Pts randomized to ICO or PBO from W0–W16 across 4 pooled phase 3 studies:



*[a]Includes pooled ICO- and PBO-randomized pts from the phase 3 ICONIC-LEAD, ICONIC-TOTAL, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2 studies. [b]Includes 66 adolescents. [c]Includes 6 adolescents. [d]ICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of which 401 were evaluable for efficacy. **BSA**=body surface area, **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **Pts**=participants, **QD**=once daily, **R**=randomization, **sPGA-G**=static Physician's Global Assessment of Genitalia, **ss-IGA**=scalp-specific IGA, **W**=week.*

Outcomes & Analyses

Response Rates Through W24

- Scalp PsO: ss-IGA score 0/1 & 0[b,c,e]
- Genital PsO: sPGA-G score 0/1 & 0[b,c,e]
- Hand/foot PsO: hf-PGA score 0/1 & 0[b,c,e]

Percent Improvement From Baseline Through W24

- Nail PsO: Modified Nail Psoriasis Severity Index (mNAPSI)[b,d,f]

AEs Through W16

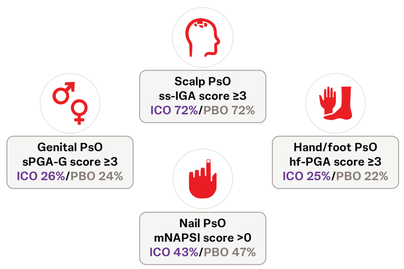
- Safety assessments for pooled ICO and PBO groups

*[a]Among pts with a score of ≥3 (at least moderate) on ss-IGA, sPGA-G, and hf-PGA, respectively, at baseline. [b]Among pts with a score of >0 on mNAPSI at baseline. [c]Nonresponder imputation / [d]No improvement from baseline assigned after pts discontinued study drug due to a lack of efficacy or an adverse event (AE) of worsening PsO, or initiated prohibited medication that could impact PsO. Observed data were used for pts who discontinued study drug for other reasons. [e]After accounting for the intercurrent events, pts with missing data were considered nonresponders. [f]The remaining missing data were not imputed. **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=icotrokinra, **mNAPSI**=Modified Nail Psoriasis Severity Index, **PBO**=placebo, **PsO**=psoriasis, **ss-IGA**=scalp-specific IGA, **sPGA-G**=static Physician's Global Assessment of Genitalia, **W**=week.*

Results

The prevalence and severity of high-impact site PsO at baseline were balanced between groups

High-Impact Site PsO Among All Pooled Randomized Pts[a] (ICO: N=1297/PBO: N=569)



Severity of High-Impact Site PsO[a]	ICO	PBO
ss-IGA score ≥3, N	935	408
Moderate (3)	80%	77%
Severe (4)	20%	23%
sPGA-G score ≥3, N	334	139
Moderate (3)	75%	68%
Severe (4)	23%	29%
Very severe (5)	2%	3%
hf-PGA score ≥3, N	319	124
Moderate (3)	80%	82%
Severe (4)	20%	18%
mNAPSI score >0, N	557	267
Mean mNAPSI score	19.8	17.2

*[a]Among pts within each category of high-impact site PsO. **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=icotrokinra, **mNAPSI**=Modified Nail Psoriasis Severity Index, **PBO**=placebo, **PsO**=psoriasis, **sPGA-G**=static Physician's Global Assessment of Genitalia, **ss-IGA**=scalp-specific IGA.*

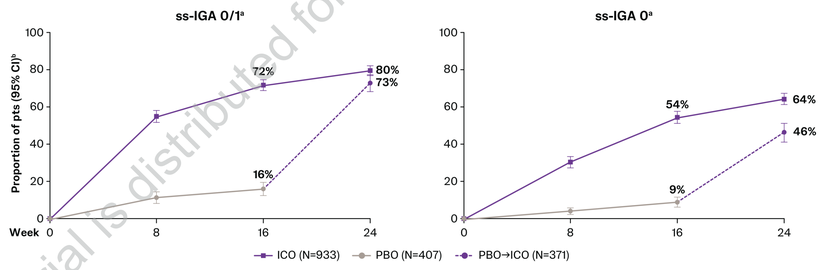
Baseline characteristics were generally similar between treatment groups within each high-impact site PsO cohort

Baseline Characteristics for Each Cohort of Pts With at Least Moderate High-Impact Site PsO	Scalp PsO: ss-IGA score ≥3		Genital PsO: sPGA-G score ≥3		Hand/foot PsO: hf-PGA score ≥3	
	ICO (N=935)	PBO (N=408)	ICO (N=334)	PBO (N=139)	ICO (N=319)	PBO (N=124)
Demographics						
Age, yrs	43.6 (14.9)	44.1 (14.6)	43.3 (13.8)	44.2 (15.0)	47.3 (14.2)	48.0 (13.6)
Female	318 (34%)	142 (35%)	103 (31%)	49 (35%)	100 (31%)	38 (31%)
Race, Asian / Black / White	21% / 2% / 75%	23% / 1% / 75%	19% / 1% / 77%	17% / 0% / 81%	22% / 3% / 72%	22% / 2% / 76%
BMI, kg/m^2	29.3 (6.5)[a]	29.3 (7.4)[a]	29.4 (6.6)[b]	29.6 (7.6)[b]	29.7 (6.6)[c]	30.2 (7.4)[c]
Disease Characteristics						
PsO duration, yrs	16.7 (12.8)	16.8 (12.7)	16.8 (13.0)	16.2 (11.3)	16.7 (12.1)	16.4 (13.1)
% of BSA with PsO	23.9 (14.9)	23.4 (15.0)	24.8 (14.7)	24.1 (15.2)	27.4 (17.7)	27.3 (17.5)
IGA score						
Moderate (3) / Severe (4)	74% / 25%	73% / 26%	73% / 26%	71% / 28%	69% / 31%	70% / 30%
PASI (0-72)	19.3 (7.7)	19.1 (7.9)	19.6 (7.6)	19.8 (7.9)	20.7 (8.9)	20.4 (9.4)
Prior PsO Treatments						
Phototherapy (PUVA and UVB)	34%	31%	35%	27%	33%	28%
Systemic therapy[d]	73%	71%	72%	75%	67%	68%
Biologic therapy[e]	30%	33%	31%	33%	26%	40%

*Data shown are mean (SD), unless otherwise noted. [a]ICO N=930/PBO N=405. [b]ICO N=333/PBO N=138. [c]ICO N=318/PBO N=123. [d]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [e]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. **BMI**=body mass index, **BSA**=body surface area, **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **Pts**=participants, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **sPGA-G**=static Physician's Global Assessment of Genitalia, **ss-IGA**=scalp-specific IGA, **UVB**=ultraviolet B.*

Scalp PsO: ICO demonstrated high rates of clearance through W24

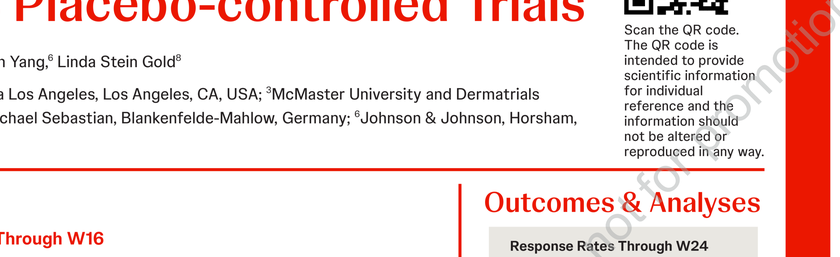
- **After transitioning to ICO at W16, PBO-randomized pts demonstrated consistent patterns of response through W24**



*ICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of which 401 were evaluable for efficacy. [a]Among pts with a baseline ss-IGA score ≥3. [b]Nonresponder imputation. Confidence intervals based on the normal approximation confidence limits. **CI**=confidence interval, **ICO**=icotrokinra, **PBO**=placebo, **pts**=participants, **ss-IGA**=scalp-specific IGA, **W**=week.*

Genital PsO: ICO demonstrated high rates of clearance through W24

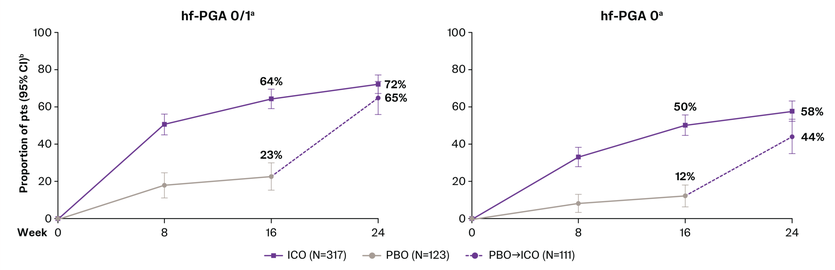
- **After transitioning to ICO at W16, PBO-randomized pts demonstrated consistent patterns of response through W24**



*ICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of which 401 were evaluable for efficacy. [a]Among pts with a baseline sPGA-G score ≥3. [b]Nonresponder imputation. Confidence intervals based on the normal approximation confidence limits. **CI**=confidence interval, **ICO**=icotrokinra, **PBO**=placebo, **pts**=participants, **sPGA-G**=static Physician's Global Assessment of Genitalia, **W**=week.*

Hand/foot PsO: ICO demonstrated high rates of clearance through W24

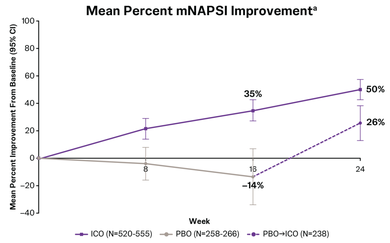
- **After transitioning to ICO at W16, PBO-randomized pts demonstrated consistent patterns of response through W24**



*ICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of which 401 were evaluable for efficacy. [a]Among pts with a baseline hf-PGA score ≥3. [b]Nonresponder imputation. Confidence intervals based on the normal approximation confidence limits. **CI**=confidence interval, **ICO**=icotrokinra, **hf-PGA**=Physician's Global Assessment of hands and feet, **PBO**=placebo, **pts**=participants, **W**=week.*

Nail PsO: ICO-randomized pts exhibited increasing mean percent mNAPSI improvement through W24

- **PBO-randomized pts demonstrated substantial improvement in nail PsO within 8 weeks of starting ICO**



*ICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of which 401 were evaluable for efficacy. [a]Among pts with a baseline mNAPSI score >0. **CI**=confidence interval, **ICO**=icotrokinra, **mNAPSI**=Modified Nail Psoriasis Severity Index, **PBO**=placebo, **PsO**=psoriasis, **pts**=participants, **W**=week.*

The ICO AE profile was similar to PBO through W16 in pts with at least moderate high-impact site PsO

Pooled Safety in Pts With at Least Moderate High-Impact Site PsO Through W16[a]	ICO (N=1068)	PBO (N=460)
Mean weeks of follow-up	15.9	15.6
Any AE	516 (48%)	233 (51%)
Serious AE	15 (1%)	9 (2%)
AE leading to discontinuation	21 (2%)	15 (3%)
Infection	252 (24%)	114 (25%)
Serious infection	0%	1 (<1%)
Malignancy	5 (<1%)	1 (<1%)

*Safety analysis set includes all randomized and treated pts. [a]Pooled phase 3 cohort with at least moderate PsO (i.e., ss-IGA, sPGA-G, and/or hf-PGA score ≥3) at ≥1 high-impact site. **AE**=adverse events, **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=icotrokinra, **PBO**=placebo, **Pts**=participants, **PsO**=psoriasis, **sPGA-G**=static Physician's Global Assessment of Genitalia, **ss-IGA**=scalp-specific IGA, **W**=week.*

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