Durability of Response to the Targeted Oral Peptide Icotrokinra for High-Impact Site Psoriasis: 1-Year ICONIC-TOTAL Findings

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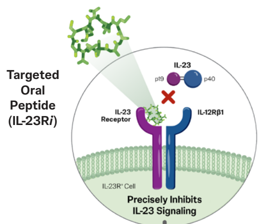
Background

Icotrokinra for plaque psoriasis (PsO)

- PsO involving difficult-to-treat, high-impact sites can have a substantial negative impact on health-related quality of life[1]
- Per the International Psoriasis Council consensus statement, PsO patients with high-impact site involvement are candidates for systemic therapy, regardless of body surface area (BSA) affected[2]
- Icotrokinra (ICO) is a first-in-class targeted oral peptide that:
  - Selectively binds the interleukin-23 receptor (IL-23R) and precisely inhibits IL-23 pathway signaling[3]
  - Demonstrated significant skin clearance, including in the scalp and genital areas, vs placebo (PBO) at Week (W)16 in participants (pts) with PsO involving high-impact sites, with similar adverse event (AE) rates vs PBO (ICONIC-TOTAL)[4]
  - Demonstrated higher rates of scalp, genital, and hand/foot PsO clearance and substantially improved nail PsO vs PBO at W16 in adults and adolescents with moderate-to-severe plaque PsO (ICONIC-LEAD)[5]

Icotrokinra Blocks IL-23 From Binding to its Receptor



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

Objective

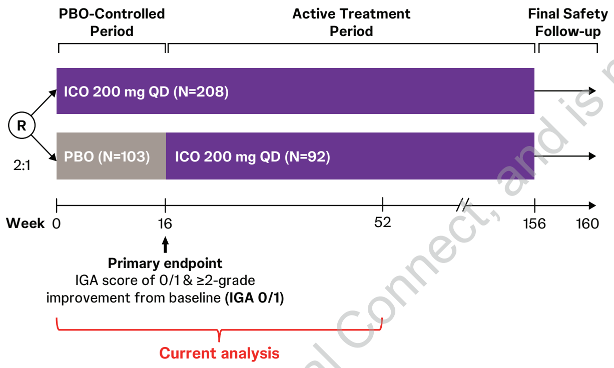
Evaluate the longer-term clinical responses and safety of ICO in adults and adolescents with PsO involving high-impact sites, including the scalp, genitals, hands/feet, and nails, from ICONIC-TOTAL through W52

ICONIC-TOTAL Study Design

Adults and adolescents with plaque PsO involving high-impact sites (N=311)

Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- BSA ≥1% and IGA score ≥2
- At least moderate (score ≥3) high-impact PsO involving ≥1 site:
  - **Scalp:** ss-IGA
  - **Genital:** sPGA-G
  - **Hand/foot:** hf-PGA
- Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical



Outcomes & Analyses

- **Overall PsO:** IGA 0/1 & 0[a,c]
- **Scalp PsO:** ss-IGA 0/1 & 0[a,c]
- **Genital PsO:** sPGA-G 0/1 & 0[a,c]
- **Hand/foot PsO:** hf-PGA 0/1 & 0[a,c]
- **Nail PsO:** mNAPSI % improvement[b,d]
- **AE:** Number (%) of pts and exposure-adjusted incidence rates (/100 PY)

[a]Nonresponder imputation / [b]0% improvement from baseline assigned after participants (pts) discontinued 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 pts who discontinued study agent for other reasons. [c]After accounting for these intercurrent events, pts with missing data were considered nonresponders. [d]The remaining missing data were not imputed.

AE=adverse event, hf-PGA=Physician's Global Assessment of hands and feet, ICO=Icotrokinra, IGA=Investigator's Global Assessment, mNAPSI=modified Nail Psoriasis Severity Index, PBO=placebo, PY=participant-years, QD=once daily, R=randomization, sPGA-G=static Physician's Global Assessment of Genitalia, ss-IGA=scalp-specific Investigator's Global Assessment.

Key Takeaways

In the phase 3 ICONIC-TOTAL study evaluating the targeted oral peptide ICO in adults and adolescents with PsO and difficult-to-treat, high-impact site involvement:

- ✓ ICO demonstrated high and durable rates of PsO clearance, with rates at W52 of:

	Clear/Almost Clear	*Completely Clear*
✓ Scalp PsO	72%	57%
✓ Genital PsO	85%	73%
✓ Hand/foot PsO	62%	58%

- ✓ ICO provided substantial mean improvement (62%) in nail PsO at W52
- ✓ ICO AE profile was similar to PBO through W16, with stable exposure-adjusted incidence rates through W52
- ✓ No ICO safety signal identified through W52

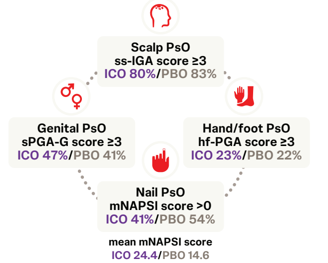
These findings support the use of ICO for the long-term management of PsO affecting high-impact sites, addressing an important unmet need with a once-daily pill

Results

Baseline pt and PsO characteristics were generally balanced between groups

Baseline Characteristics	ICO (N=208)	PBO (N=103)
Demographics		
Age, yrs	45.3 (14.6)	43.5 (13.8)
Female	34%	39%
Race, Asian/Black/White	20% / 1% / 77%	19% / 0% / 80%
BMI, kg/m²	29.0 (6.6)[a]	29.4 (8.1)[a]
Disease Characteristics		
PsO duration, yrs	16.8 (13.3)	15.2 (10.5)
% BSA with PsO	16.6 (13.5)	14.8 (11.7)
IGA score		
Moderate (3)	74%	71%
Severe (4)	22%	21%
PASI (0–72)	14.6 (7.6)	14.0 (7.0)
Prior PsO Treatments		
Phototherapy[b]	43%	31%
Systemic therapy[c]	73%	73%
Biologic therapy[d]	34%	31%

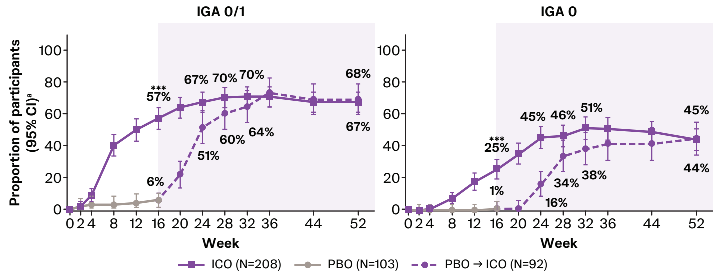
Pts With High-Impact Site PsO at Baseline



Data shown are mean (SD) unless otherwise noted. PsO involving high-impact sites was not mutually exclusive. [a]ICO: N=203; PBO: N=101. [b]PUVA and UVB. [c]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [d]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, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PBO**=placebo, **PsO**=psoriasis, **PASI**=Psoriasis Area and Severity Index, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **UVB**=ultraviolet B.

Overall PsO: ICO demonstrated high rates of clearance that were durable through W52

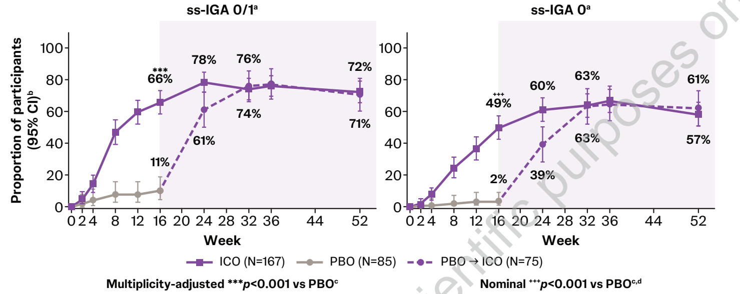
- After transitioning to ICO, PBO-randomized pts achieved skin PsO clearance rates comparable to ICO-randomized pts



[a]Nonresponder imputation. [b]P-values based on Cochran-Mantel-Haenszel chi-square test stratified by high-impact site involvement and BSA category. **CI**=confidence interval, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PBO**=placebo.

Scalp PsO: ICO demonstrated high rates of clearance that were durable through W52

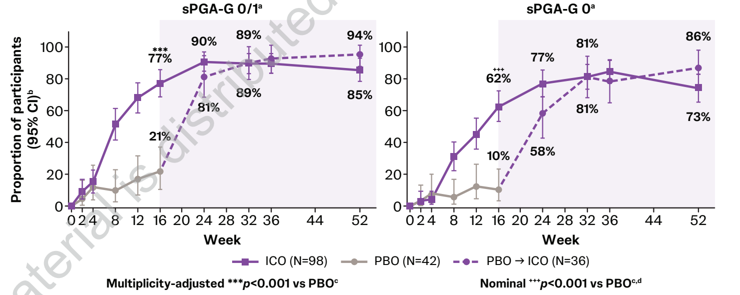
- After transitioning to ICO, PBO-randomized pts achieved scalp PsO clearance rates comparable to ICO-randomized pts



[a]Among pts with a baseline ss-IGA score ≥3. [b]Nonresponder imputation. [c]P-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and BSA category. [d]Endpoint was not included in the hierarchical testing strategy. **BSA**=body surface area, **CI**=confidence interval, **ICO**=Icotrokinra, **PBO**=placebo, **pts**=participants, **ss-IGA**=scalp-specific Investigator's Global Assessment.

Genital PsO: ICO demonstrated high rates of clearance that were durable through W52

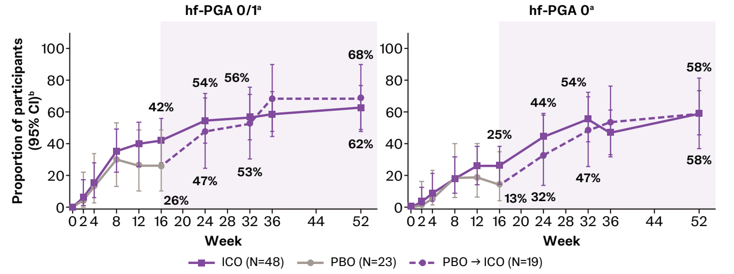
- After transitioning to ICO, PBO-randomized pts achieved genital PsO clearance rates comparable to ICO-randomized pts



[a]Among pts with a baseline sPGA-G score ≥3. [b]Nonresponder imputation. [c]P-values based on Cochran-Mantel-Haenszel chi-square test stratified BSA category. [d]Endpoint was not included in the hierarchical testing strategy. **BSA**=body surface area, **CI**=confidence interval, **ICO**=Icotrokinra, **PBO**=placebo, **sPGA-G**=static Physician's Global Assessment of Genitalia.

Hand/foot PsO: ICO demonstrated increasing rates of clearance through W52

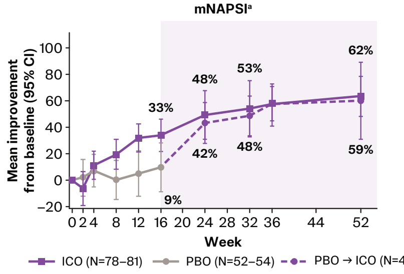
- After transitioning to ICO, PBO-randomized pts achieved hand/foot PsO clearance rates comparable to ICO-randomized pts



[a]Among pts with a baseline hf-PGA score ≥3. [b]Nonresponder imputation. **CI**=confidence interval, **ICO**=Icotrokinra, **hf-PGA**=Physician's Global Assessment of hands and feet, **PBO**=placebo, **pts**=participants.

Nail PsO: ICO provided substantial mean improvement (62%) at W52

- After transitioning to ICO, PBO-randomized pts achieved improvements in nail PsO comparable to ICO-randomized pts



[a]Among pts with a baseline mNAPSI score >0. **CI**=confidence interval, **ICO**=Icotrokinra, **mNAPSI**=modified Nail Psoriasis Severity Index, **PBO**=placebo.

Exposure-adjusted AE rates were consistent across groups and study phases

- ICO AE profile was similar to PBO through W16; no ICO safety signal identified through W52

AEs Through W52	PBO-controlled (W0–16) ICO (N=208)	PBO-controlled (W0–16) PBO (N=103)	W16–52 PBO→ICO (N=92)	Through W52 ICO (N=208)	Through W52 ICO Combined[a] (N=300)
Mean Weeks / Total PY of Follow-Up	16.0 / 63.6	15.6 / 30.8	36.2 / 63.9	49.3 / 196.4	45.3 / 260.2
Any AE	105 (50%)	46 (45%)	51 (55%)	153 (74%)	204 (68%)
Incidence/100 PY (95% CI)[b]	233 (188, 277)	217 (154, 280)	132 (96, 168)	169 (142, 195)	158 (136, 179)
SAE	1 (<1%)	2 (2%)	1 (1%)	6 (3%)	7 (2%)
Incidence/100 PY (95% CI)[b]	2 (0, 5)	7 (0, 16)	2 (0, 5)	3 (1, 6)	3 (1, 5)
AE Leading to D/C	6 (3%)	4 (4%)	0 (0%)	7 (3%)	7 (2%)
Incidence/100 PY (95% CI)[c]	10 (4, 21)	13 (4, 34)	0 (0, 5)	4 (1, 7)	3 (1, 6)
Infection	59 (28%)	23 (22%)	39 (42%)	106 (51%)	145 (48%)
Incidence/100 PY (95% CI)[b]	110 (82, 138)	88 (52, 124)	81 (56, 106)	81 (66, 96)	81 (68, 94)
Serious Infection	0 (0%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)
Incidence/100 PY (95% CI)[c]	0 (0, 5)	3 (<1, 18)	0 (0, 5)	0 (0, 2)	0 (0, 1)
GI AE	15 (7%)	8 (8%)	7 (8%)	21 (10%)	28 (9%)
Incidence/100 PY (95% CI)[b]	25 (12, 37)	27 (8, 46)	11 (3, 20)	12 (7, 17)	12 (7, 16)
Malignancy[d]	1 (<1%)	0 (0%)	0 (0%)	2 (1%)	2 (1%)
Incidence/100 PY (95% CI)[c]	2 (<1, 9)	0 (0, 10)	0 (0, 5)	1 (<1, 4)	1 (<1, 3)

Data shown are n (%) unless otherwise noted. [a]Includes data for ICO-randomized pts through W52 and for PBO-to-ICO pts from W16 through W52. [b]CIs were based on a Wald statistic using the normal assumption. [c]CIs were based on an exact method assuming that the observed number of events follows a Poisson distribution. [d]Includes chronic lymphocytic leukaemia and malignant melanoma in situ. **AE**=adverse event, **CI**=confidence interval, **D/C**=discontinuation, **GI**=gastrointestinal, **ICO**=Icotrokinra, **PBO**=placebo, **PY**=participant-years, **SAE**=serious AE, **W**=week.

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