Durability and Safety of the Targeted Oral Peptide Icotrokinra for High-Impact Site Psoriasis: 2-Year ICONIC-TOTAL Findings

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Background

Plaque psoriasis (PsO) is a chronic inflammatory disease that may involve high-impact sites, such as the scalp, genitals, hands/feet, and nails

- High-impact site plaque PsO can be difficult to treat and has a significant impact on health-related quality of life[1]

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

- Precisely targets the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[2]
- Demonstrated robust efficacy and a favorable safety profile versus placebo (PBO) through Week (W) 16,[3,4] with consistent results through 1 year[5-8]

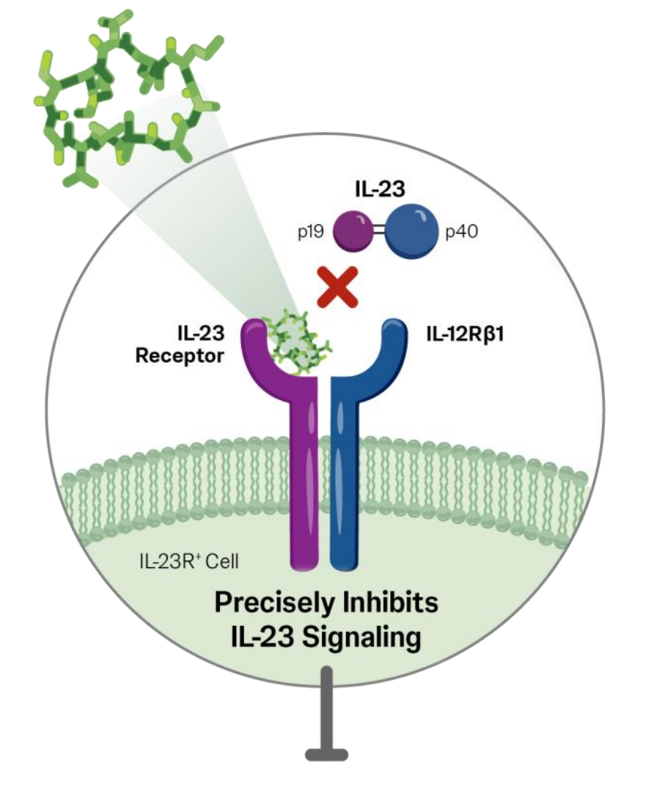
ICONIC-TOTAL (NCT06095102)

- Ongoing, phase 3, multicenter, randomized, double-blind, PBO-controlled trial in adult and adolescent participants (pts; ≥12 years of age)
- Long-term data on durability of response and safety will help inform treatment decisions

Objectives

Report clinical response rates and safety of ICO through 2 years in ICONIC-TOTAL study pts with high-impact site plaque PsO

Icotrokinra Blocks IL-23 From Binding to its Receptor


IL-23
p19
p40
IL-23 Receptor
IL-12Rβ1
IL-23R+ Cell
Precisely Inhibits IL-23 Signaling
Inhibits IL-17A, IL-17F, and IL-22 Production

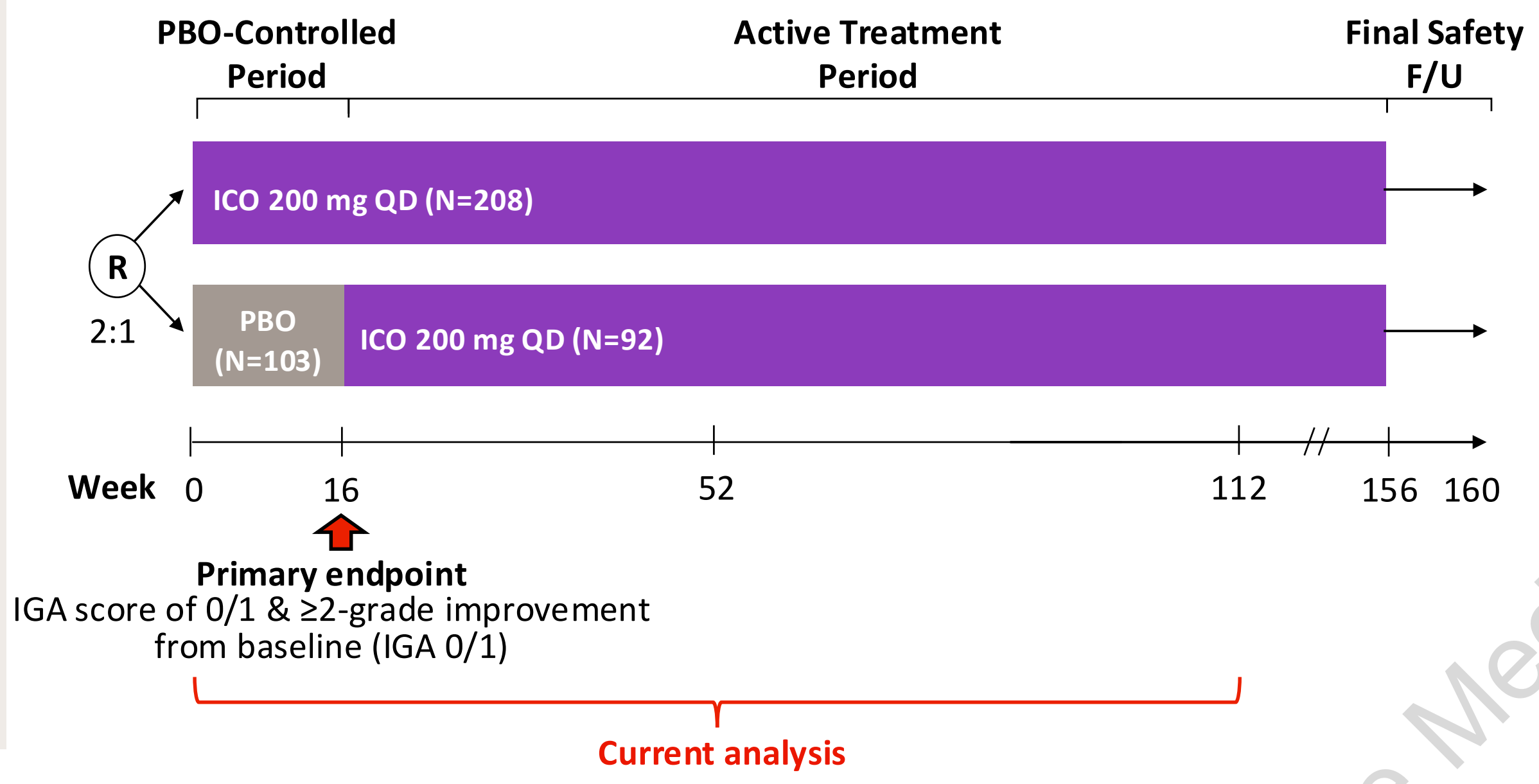
IL-12Rβ1=interleukin-12 receptor beta 1, IL-23R=interleukin-23 receptor.

ICONIC-TOTAL Study Design

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

Key inclusion criteria

- ≥12 years of age
- 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 treatment



AE=adverse event, BSA=body surface area, CI=confidence interval, F/U=follow-up, hf-PGA=Physician's Global Assessment of hands and feet, IGA=Investigator's Global Assessment, mNAPSI=modified Nail Psoriasis Severity Index, PY=patient-year, QD=once daily, R=randomization, sPGA-G=static Physician's Global Assessment of Genitalia, ss-IGA=scalp-specific Investigator's Global Assessment.

Outcomes & Analyses

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

[a]Through W52 nonresponder imputation / [b]0% improvement from baseline assigned after 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 W52 nonresponder imputation / [d]0% improvement from baseline assigned after pts who discontinued study drug due to a lack of efficacy or an AE of worsening PsO. [e]After accounting for these intercurrent events: through W52 pts with missing data were considered nonresponders and, after W52, other missing data were imputed using multiple imputation. [f]The remaining missing data were not imputed.

Key Takeaways

- ✓ Through W112, among adults and adolescents with high-impact site PsO in the phase 3 ICONIC-TOTAL study, ICO demonstrated:
  - ✓ High and durable rates of overall and high-impact site PsO clearance
  - ✓ An AE profile similar to PBO through W16 with no new safety signals identified through W112
- ✓ The robust efficacy and favorable safety profile through 2 years support the use of the once-daily targeted oral peptide ICO for long-term management of high-impact site PsO

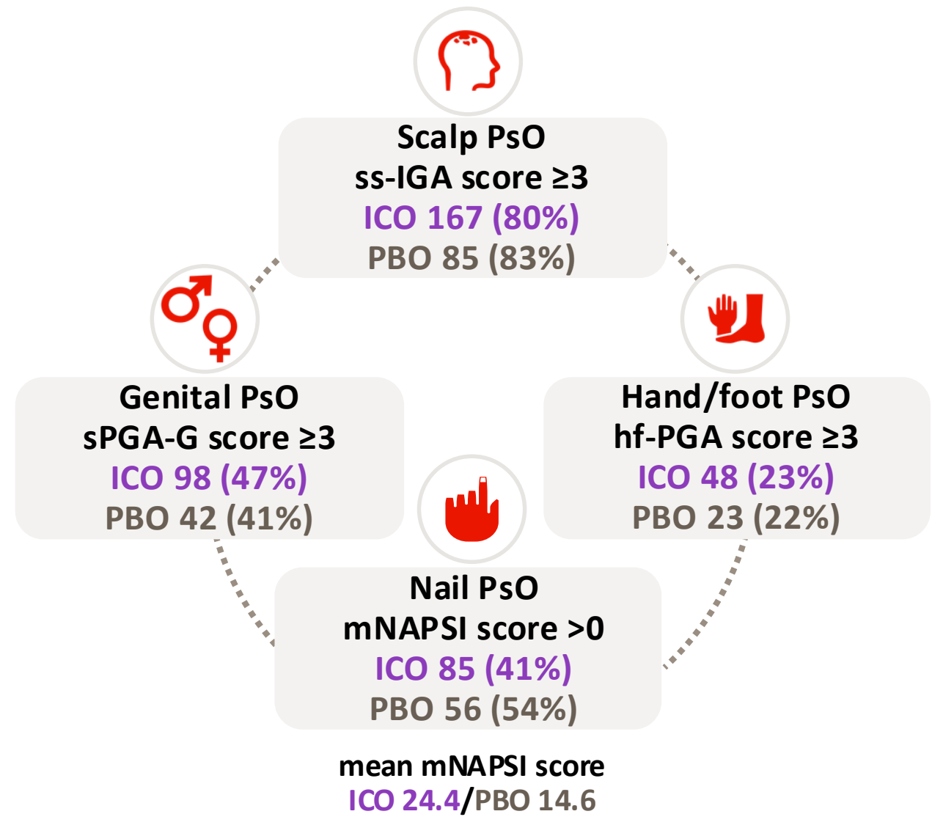
Results

Baseline demographics and PsO characteristics were generally balanced between groups

- Among pts with hf-PsO at baseline, greater proportions of pts in the ICO (35%) group had severe hand/foot PsO (hf-PGA=4) compared with PBO (17%)

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)[b]
Disease Characteristics		
PsO disease 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[c]	43%	31%
Systemic therapy[d]	73%	73%
Biologic therapy[e]	34%	31%

Pts With High-Impact Site PsO at Baseline



Scalp PsO
ss-IGA score ≥3
ICO 167 (80%)
PBO 85 (83%)

Genital PsO
sPGA-G score ≥3
ICO 98 (47%)
PBO 42 (41%)

Hand/foot PsO
hf-PGA score ≥3
ICO 48 (23%)
PBO 23 (22%)

Nail PsO
mNAPSI score >0
ICO 85 (41%)
PBO 56 (54%)

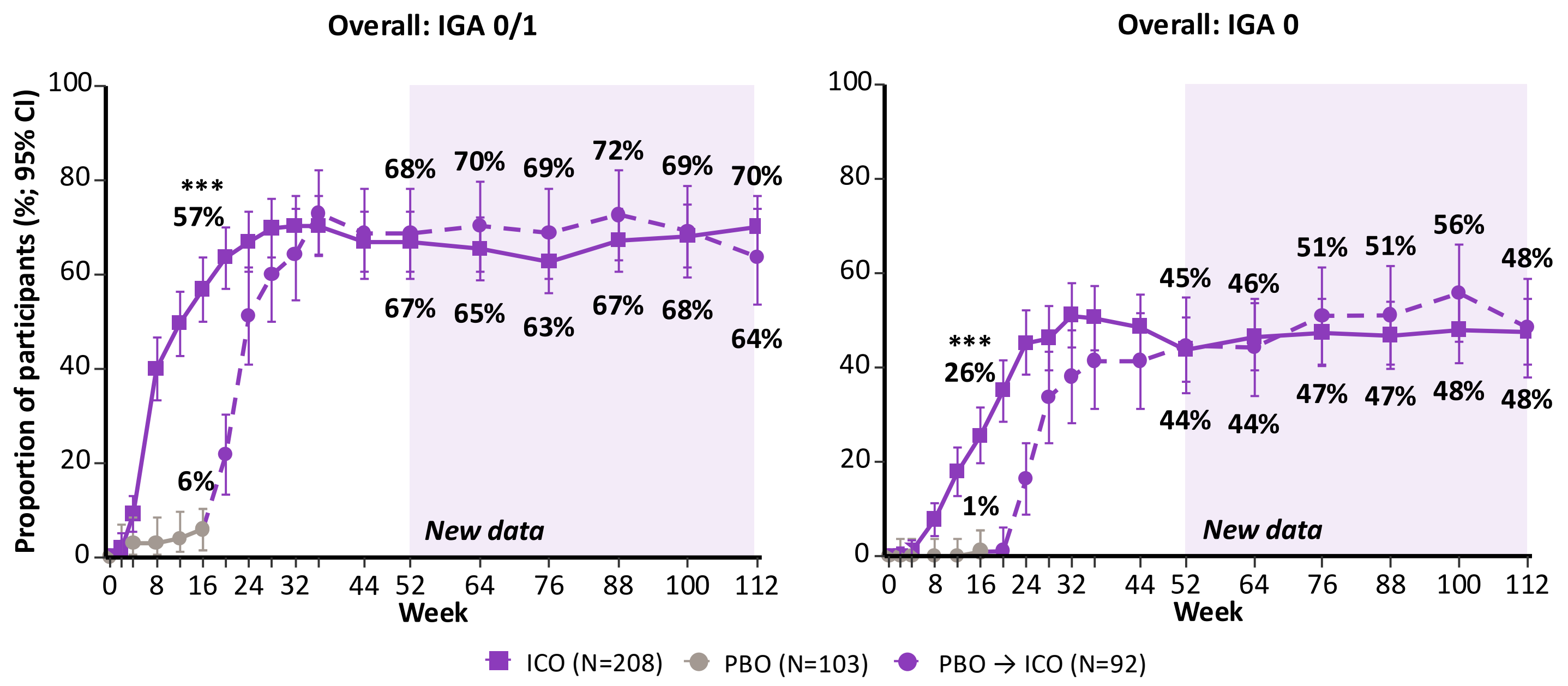
mean mNAPSI score
ICO 24.4/PBO 14.6

*Data shown are mean (SD) unless otherwise noted. PsO involving high-impact sites was not mutually exclusive. [a]N=203. [b]N=101. [c]PUVA and UVB. [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, **PASI**=Psoriasis Area and Severity Index, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **UVB**=ultraviolet B, **yrs**=years.*

Overall PsO: IGA 0/1 response rates increased through W24 (67%) and remained stable through W112 (70%) among ICO-randomized pts

- IGA 0 response rates also increased through W24 (45%) and were consistent through W112 (48%) among ICO-randomized pts

Overall: IGA 0/1 | **Overall: IGA 0**



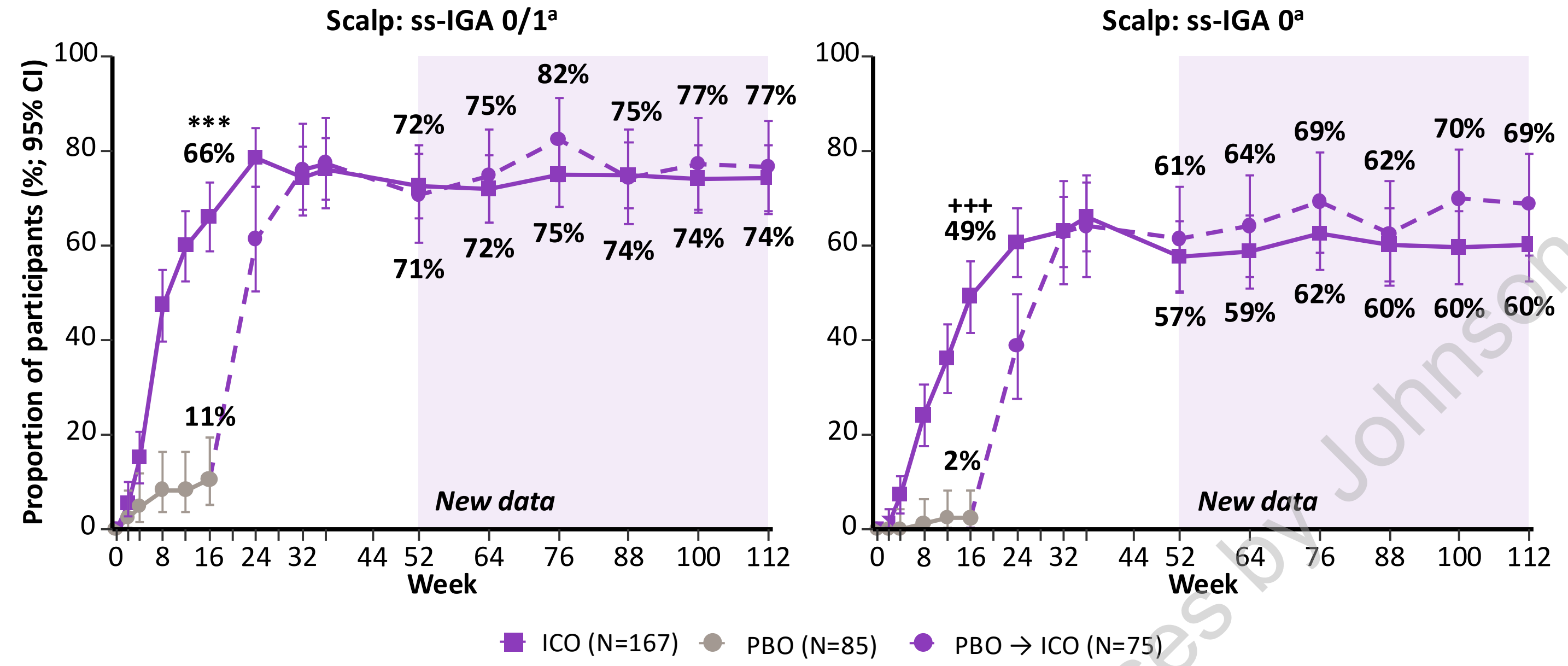
Multiplicity-adjusted *****p*<0.001 vs PBO[a]

[a]p-values based on Cochran-Mantel-Haenszel chi-square test stratified by high-impact site involvement and BSA category.

Scalp PsO: ss-IGA 0/1 response rates increased through W24 (78%) and remained stable through W112 (74%) among ICO-randomized pts

- ss-IGA 0 response rates also increased through W24 (60%) and were consistent through W112 (60%) among ICO-randomized pts

Scalp: ss-IGA 0/1[a] | **Scalp: ss-IGA 0[a]**



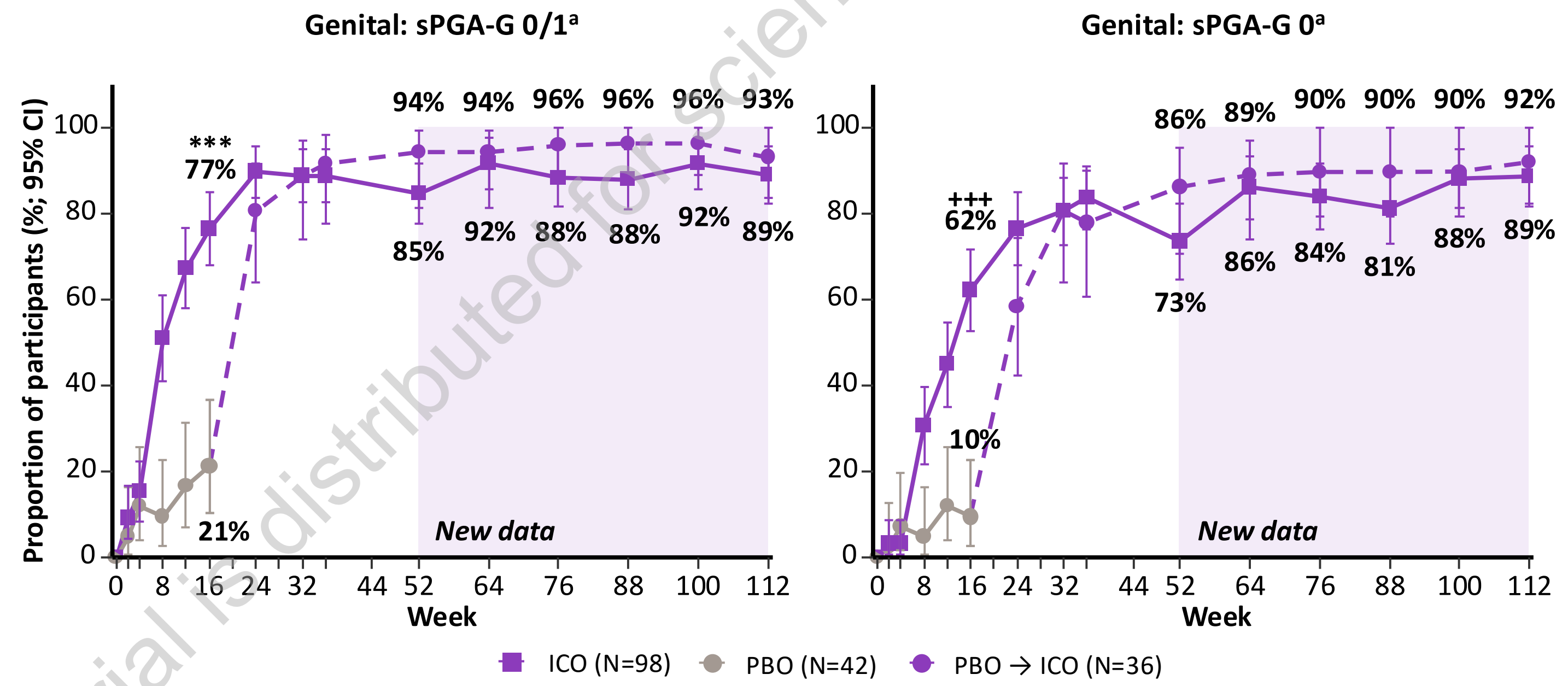
Multiplicity-adjusted *****p*<0.001 vs PBO[b] | **Nominal +++*p*<0.001 vs PBO[b,c]**

[a]Among pts with a baseline ss-IGA score ≥3. [b]p-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and BSA category. [c]Endpoint was not included in the hierarchical testing strategy.

Genital PsO: sPGA-G 0/1 response rates increased through W24 (90%) and remained stable through W112 (89%) among ICO-randomized pts

- 89% of ICO-randomized pts achieved completely clear genital PsO (sPGA-G 0) at W112

Genital: sPGA-G 0/1[a] | **Genital: sPGA-G 0[a]**



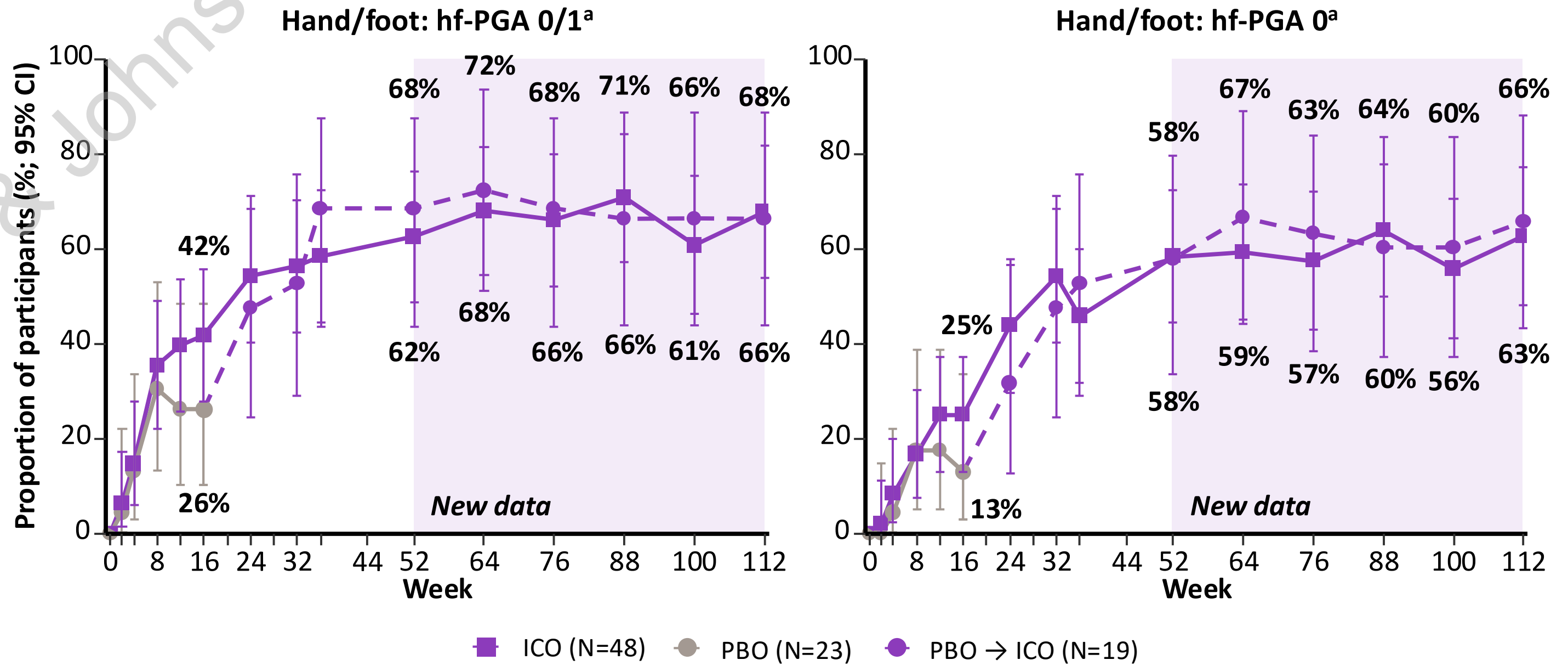
Multiplicity-adjusted *****p*<0.001 vs PBO[b] | **Nominal +++*p*<0.001 vs PBO[b,c]**

[a]Among pts with a baseline sPGA-G score ≥3. [b]p-values based on Cochran-Mantel-Haenszel chi-square test stratified BSA category. [c]Endpoint was not included in the hierarchical testing strategy.

Hand/foot PsO: hf-PGA 0/1 response rates increased through W24 (54%) and remained stable through W112 (68%) among ICO-randomized pts

- 63% of ICO-randomized pts achieved completely clear hand/foot PsO (hf-PGA 0) at W112

Hand/foot: hf-PGA 0/1[a] | **Hand/foot: hf-PGA 0[a]**

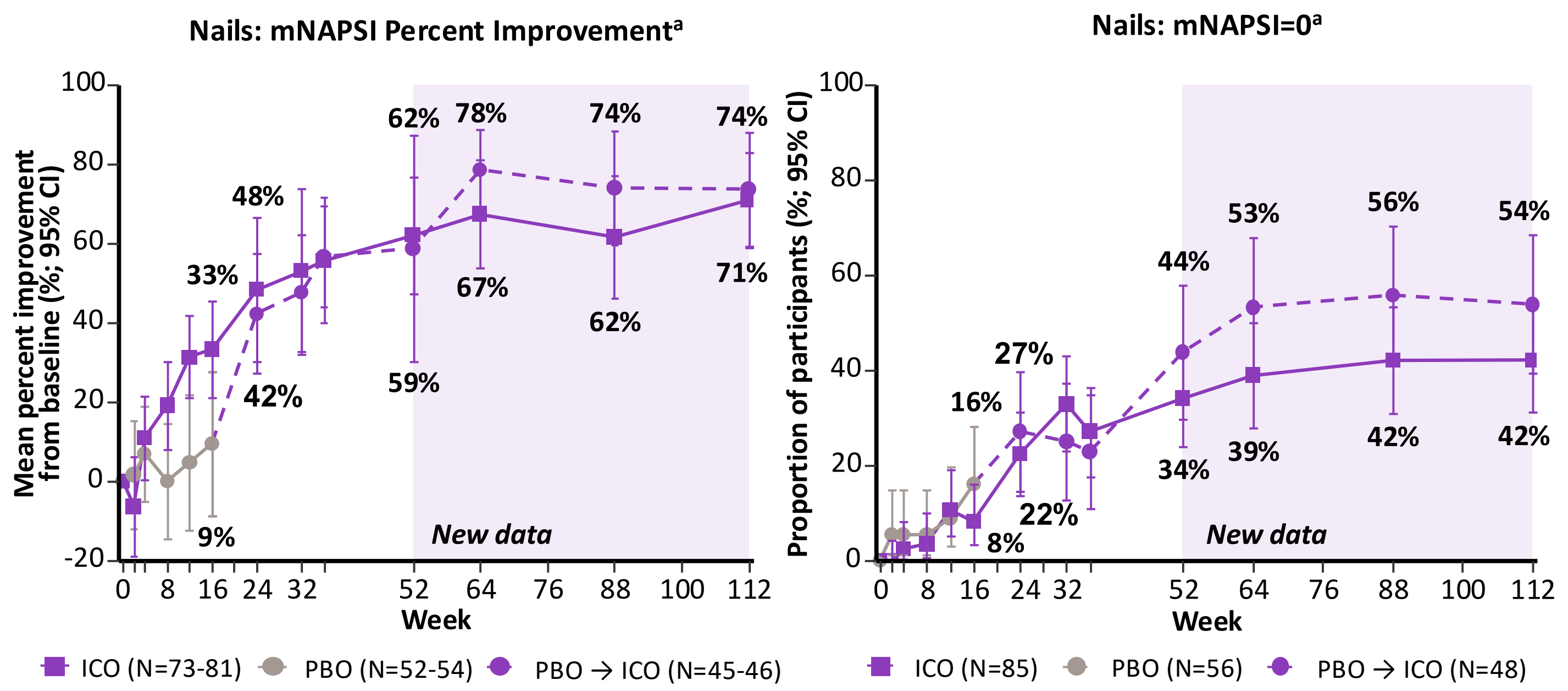


[a]Among pts with a baseline hf-PGA score ≥3.

Nail PsO: ICO demonstrated increasing improvements through W64 (67%), which were consistent through W112 (71%)

- 42% of ICO-randomized pts achieved completely clear nail PsO (mNAPSI=0) at W112

Nails: mNAPSI Percent Improvement[a] | **Nails: mNAPSI=0[a]**



[a]Among pts with a baseline mNAPSI score >0.

Exposure-adjusted AE rates were consistent across treatment groups and study phases through W112

- ICO AE profile was similar to PBO through W16, with no increases in exposure-adjusted rates through 2 years of treatment

AEs Through W112	PBO-controlled (W0-16)		W0-52	W0-W112
	ICO (N=208)	PBO (N=103)	ICO Combined[a] (N=300)	ICO Combined[a] (N=300)
Mean weeks / total PY of follow-up	15.9 / 63.3	15.5 / 30.6	45.0 / 258.9	98.1 / 563.9
Any AE	105 (50%)	46 (45%)	206 (69%)	240 (80%)
Incidence/100PY (95% CI)[b]	232 (188, 277)	219 (156, 282)	160 (138, 182)	122 (106, 137)
SAE	1 (<1%)	2 (2%)	7 (2%)	15 (5%)
Incidence/100PY (95% CI)[b]	2 (0, 9)	7 (1, 24)	3 (1, 6)	3 (1, 4)
AE leading to D/C	6 (3%)	4 (4%)	7 (2%)	10 (3%)
Incidence/100PY (95% CI)[c]	10 (4, 21)	13 (4, 34)	3 (1, 6)	2 (1, 3)
Infection	59 (28%)	23 (22%)	146 (49%)	180 (60%)
Incidence/100PY (95% CI)[b]	110 (82, 138)	89 (53, 126)	82 (69, 95)	58 (50, 67)
Serious infection	0 (0%)	1 (1%)	0 (0%)	2 (1%)
Incidence/100PY (95% CI)[b]	0 (0, 5)	3 (<1, 18)	0 (0, 1)	<1 (0, 1)
GI AE	15 (7%)	8 (8%)	28 (9%)	49 (16%)
Incidence/100PY (95% CI)[b]	25 (12, 38)	27 (12, 54)	12 (7, 16)	10 (7, 12)
Malignancy[c]	1 (<1%)	0 (0%)	2 (1%)	6 (2%)
Incidence/100PY (95% CI)[b]	2 (0, 9)	0 (0, 10)	1 (<1, 3)	1 (<1, 2)

*Data shown are n (%) unless otherwise noted. [a]Includes data for ICO-randomized pts through W52 and for PBO → ICO pts from W16 through W52/W112. [b]CI is based on the normal approximation or an exact method following a Poisson distribution if the number of pts with events is <10. [c]Includes one of basal cell carcinoma, chronic lymphocytic leukemia, malignant melanoma stage 0, prostate cancer, squamous cell carcinoma and squamous cell carcinoma of the cervix. **D/C**=discontinuation, **GI**=gastrointestinal, **SAE**=serious AE.*

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