

Key Takeaways

- Substantial improvements in PsA disease activity and pain, overall PsO, nail and scalp PsO, as well as HRQoL that were durable through W52

Acknowledging the inherent limitations of post hoc subgroup analyses, these findings further support the potential of ICO as a targeted oral treatment option for active PsA

Isotrokinra (ICO), the first and only targeted oral peptide:

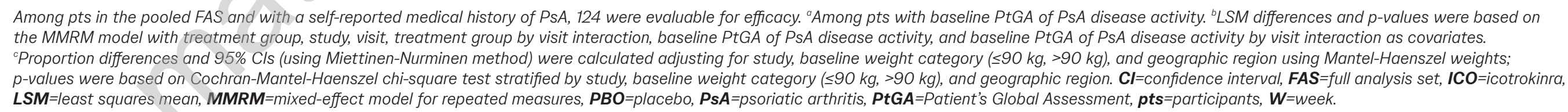
- Precisely blocks the interleukin (IL)-23 receptor and inhibits IL-23 signaling¹
- Approved for the treatment of moderate-to-severe plaque psoriasis (PsO) in adults and pediatric patients (≥12 years, ≥40 kg) who are candidates for systemic therapy or phototherapy²
- Demonstrated substantial improvements in psoriatic arthritis (PsA) disease activity/pain, psoriasis PsA, and high rates of psoriasis PsA

Objective

Results

Data shown are mean (SD), unless otherwise noted. [†]ICO N=86/PBO N=34. [‡]Among pts with a baseline f-PGA score > 0: ICO N=47/PBO N=19. [§]ICO N=86/PBO N=36. BMI=body mass index, BSA=body surface area, DLQI=Dermatology Life Quality Index, f-PGA=fingertip Physical Global Assessment, HRQoL=health-related quality of life, ICO=iclotrocin, IG=investigator's Global Assessment, mNAPS=modified Nail Psoriasis Severity Index, PASI=Psoriasis Area and Severity Index, PBO=placebo, PsA=psoriatic arthritis, PsO=psoriasis, PiGA=Patient's Global Assessment, pts=participants, SD=standard deviation, ss-IGA=Scalp-Specific Investigator's Global Assessment, yrs=years.

- ~50% of ICO-randomized pts reported ≥50% improvement in PsA disease activity at W16, with durable response rates through W52



Key inclusion criteria

- ≥18 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥10%
- Psoriasis Area and Severity Index (PASI) score ≥12
- Investigator's Global Assessment (IGA) score ≥3
- Candidate for phototherapy or systemic therapy for plaque PsO

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

PBO-Controlled W0–W16

ICONIC-ADVANCE 1[†] (N=467) 2:1

ICONIC-ADVANCE 2[†] (N=404*) 4:1

Week 0 2 4 8 12 16 20 24 28 32 36 44 52

ICO 200 mg QD

PBO

ICO 200 mg QD

Current Analysis

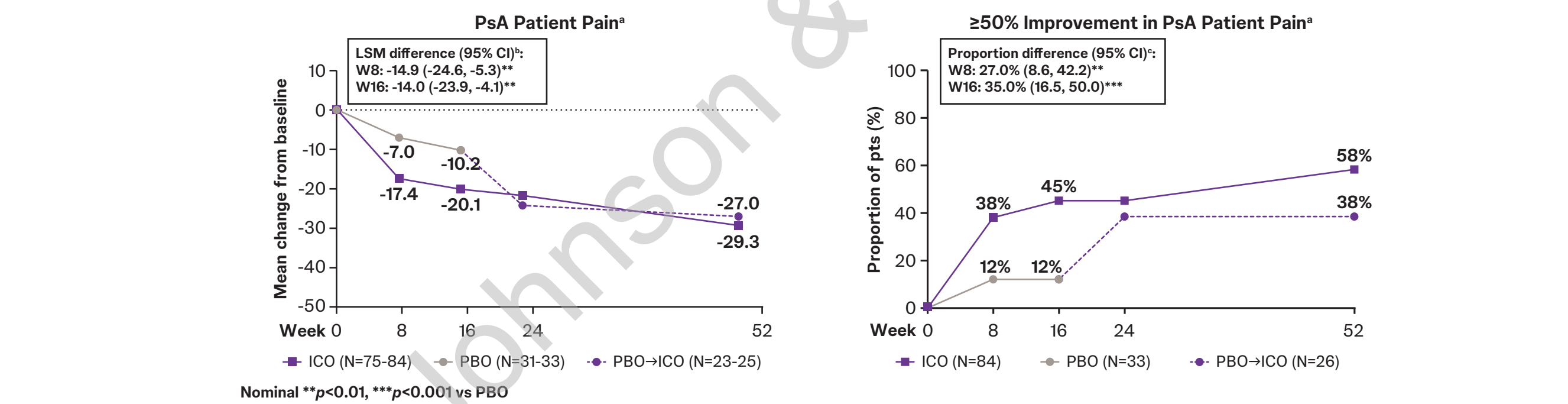
Pooled FAS* AND a self-reported medical history of PsA (N=127: ICO, N=89; PBO, N=38)*

^aICONIC-ADVANCE 2 enrolled 404 pts in the ICO and PBO groups, of whom 401 were evaluable for efficacy. ^bIncludes pooled ICO- and PBO-randomized pts from the phase 3 ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 studies. ^cAmong pts in the pooled FAS and with a self-reported medical history of PsA, 124 were evaluable for efficacy. **FAS**=full analysis set, **ICO**=iclotrokinra, **PBO**=placebo, **PsA**=psoriatic arthritis, **PsO**=psoriasis, **pts**=participants, **QD**=once daily, **R**=randomization, **W**=week.

PsA-Specific PROs (VAS): ● Mean change from baseline in PtGA of PsA disease activity and in PsA Patient Pain^{a,c} ● ≥50% improvement from baseline in PtGA of PsA disease activity and in PsA Patient Pain^{b,d,e} Overall/High-Impact Site PsO: ● Mean/median percent improvement from baseline in PASI^{a,c} ● Mean percent improvement from baseline in mNAPSI (among pts with a baseline mNAPSI score >0)^{a,c} ● f-PGA 0/1 and 0 (among pts with a baseline f-PGA score ≥2)^{b,d} ● ss-IGA 0/1 and 0 (among pts with a baseline ss-IGA score ≥2)^{b,d}	HRQoL: ● DLQI 0/1 (among pts with a baseline DLQI score >1)^{b,d} AEs: ● Safety assessments through W16 and through W52
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IS-GRA 01 reflects score 01 at end 24-grade improvement from baseline. *No improvement from baseline. †Nonresponse imputation assigned after study discontinued study drug due to a lack of efficacy of 01 or 04 worsening PAIN or initiated prohibited medication that could impact PAIN. Secondary end points were used for study to discontinued study drug for other reasons. The remaining missing data were not imputed. ‡After accounting for the intervention effects, study with missing data were categorized nonresponders. §30% improvement from baseline in PAIN at PAIN 01 and PAIN Patient Pain represent components of American College of Rheumatology Study 50 (ACRSO) response criteria, a stringent, clinically relevant measure of improvement in PAIN. ¶AE=adverse event. DQW=dermatology life quality index. F-PGA=Primary Physician's Global Assessment of Pain with related quality life. mPAIN=modified Pain Catastrophizing Severity index. PBO=patient-reported outcome. PAIN Patient Pain Patient's Assessment of Pain. PAIN PAIN=global assessment. vs-ISA=vs-symptom-specific investigator's Global Assessment. VAS=visual analog scale.

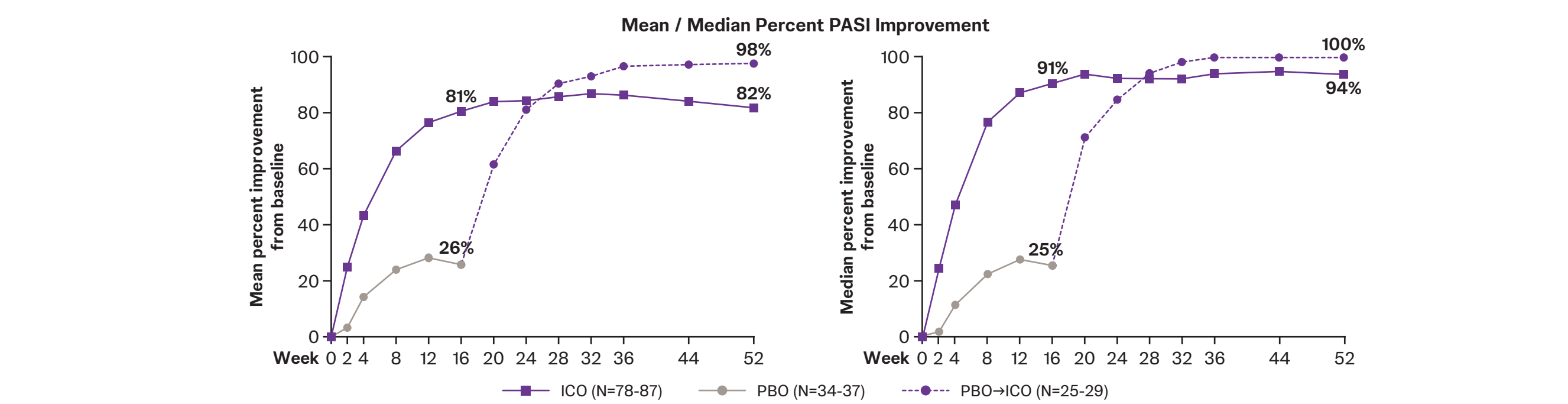
- Nearly one-half of ICO-randomized pts reported $\geq 50\%$ improvement in PsA Patient Pain at W16, with durable response rates through W52



Among pts in the pooled FAS and with a self-reported medical history of PSA, 124 were evaluable for efficacy. Among pts with baseline PSA Patient Pain, LSM differences and p-values were based on the MMRM model with treatment group, study, visit, treatment group by visit interaction, baseline PSA Patient Pain, and baseline PSA Patient Pain by visit interaction as covariates. Proportion differences and 95% CIs (using Miettinen-Nurminen method) were calculated adjusting for study, baseline weight category (≤ 90 kg, >90 kg), and geographic region using Mantel-Haenszel weights; p-values were based on Cochran-Mantel-Haenszel chi-square test stratified by study, baseline weight category (≤ 90 kg, >90 kg), and geographic region. **CI**=confidence interval, **FAS**=full analysis set, **ICO**=icotrokin, **LSM**=least squares mean, **MMRM**=mixed-effects model for repeated measures, **PBO**=placebo, **PSA**=prostate-specific antigen, **pts**=participants, **W**=week.

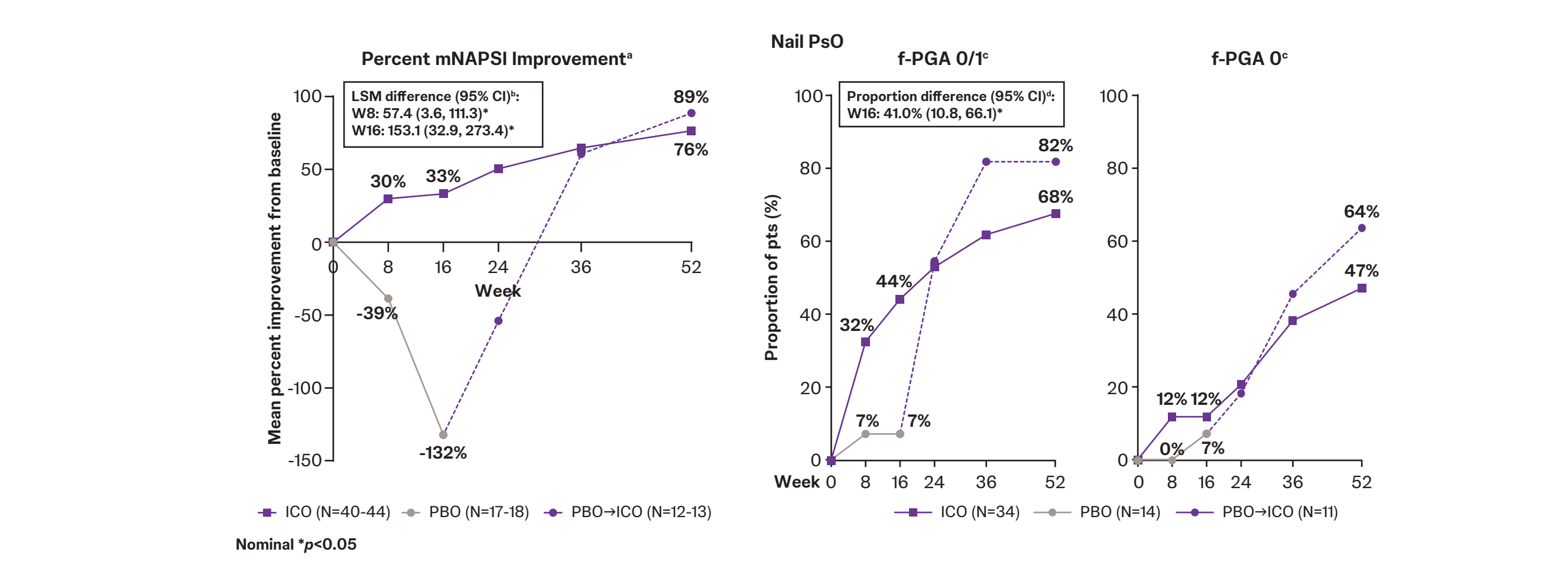
- ICO showed separation from PBO as early as W2 (LSM difference: 21.1 [95% CI: 12.6, 29.6]; nominal $p < 0.001^a$)

- ICO demonstrated greater LSM percent PASI improvement from baseline vs PBO at W16 (81% vs 26%, respectively; LSM difference: 55.2 [95% CI: 42.8, 67.7]; nominal $p < 0.001^*$)



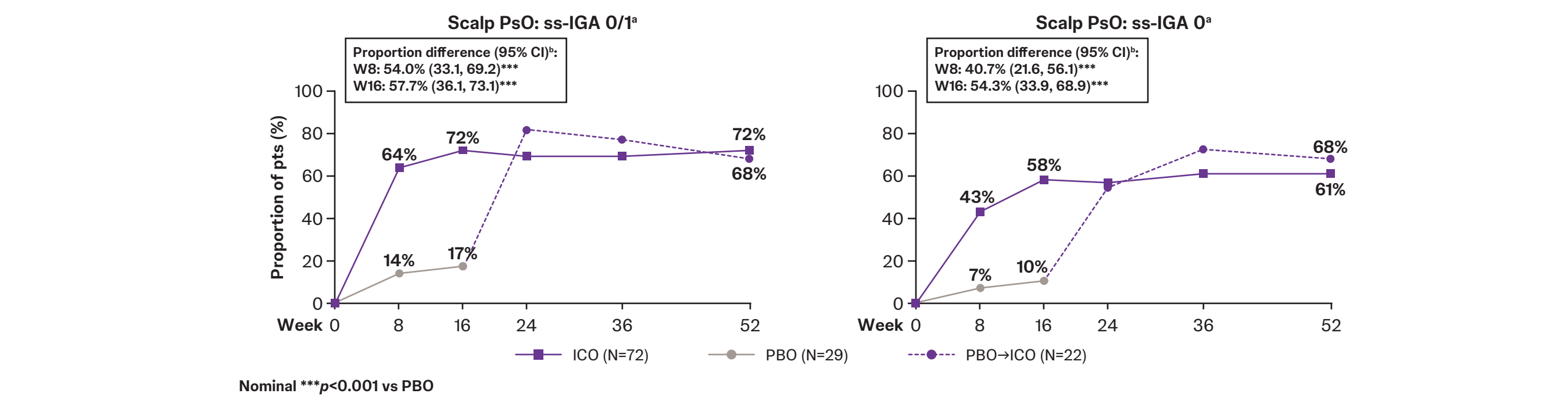
Among pts in the pooled FAS and with a self-reported medical history of PsA, 124 were evaluable for efficacy. *LSMs, LSM differences, and p-values were based on the MMRM model with treatment group, study, treatment group by visit interaction, baseline PASI total score, and baseline PASI total score by visit interaction as covariates. FAS—full analysis set, ICO—icatrantra, LSM—least squares mean, MMRM—mixed-effects model for repeated measures, PASI—Psoriasis Area and Severity Index, PBO—placebo, PsA—psoriatic arthritis.

- Nearly 70% of ICO-randomized pts achieved clear/almost clear nail PsO at W52



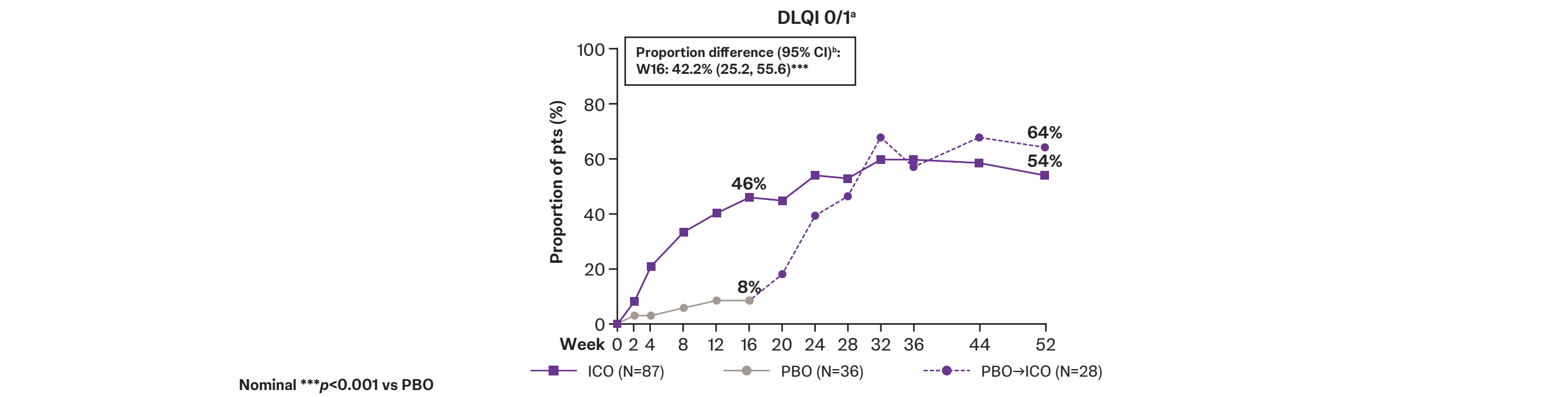
Among pts in the pooled FAS and with a self-reported medical history of PTA, 124 were evaluable for efficacy. Among pts with a baseline mNAPSI score ≥ 0 , LSM differences and p-values were based on the MM model with treatment group, study, visit, treatment group by visit interaction, baseline mNAPSI score, and baseline mNAPSI score by visit interaction as covariates. Among pts with a baseline fPGA score ≥ 2 , "Proportion difference and 95% CI (using Mettinen-Nurminen method) were calculated adjusting for study, baseline weight category (≤ 90 kg, >90 kg), and geographic region using Mantel-Haenszel weights; p-values were based on Cochran-Mantel-Haenszel chi-square test stratified by study, baseline weight category (≤ 90 kg, >90 kg), and geographic region. CI=confidence interval, fPGA=fingert Physician's Global Assessment. ICO=ictrosol, LSM=least-squares mean, mNAPSI=modified Nail Psoriasis Severity index, PBO=placebo, Pto=psoriasis, pts=participants, W=week.

- 72% of ICO-randomized pts achieved clear/almost clear scalp PsO at W52



Among *pts* in the pooled FAS and with a self-reported medical history of PsA, 124 were evaluable for efficacy. Among *pts* with a baseline ss-IGA score ≥ 2 , "Proportion differences and 95% CI" (using Miettinen-Nurminen method) were calculated adjusting for study, baseline weight category (≤ 90 kg, >90 kg), and geographic region using Mantel-Haenszel weights; *p*-values were based on Cochran-Mantel-Haenszel chi-square test stratified by study, baseline weight category (≤ 90 kg, >90 kg), and geographic region. CI=confidence interval. FAS=full analysis set. ICO=ictr03krva. PBO=placebo. PsA=psoriatic arthritis. PsO=psoriasis. *pts*=participants. ss-IGA/II=ss-IGA score 0/I and ≥ 2 score improvement from baseline. W=week.

- ICO showed separation from PBO as early as W4 (proportion difference: 19.8% [95% CI: 6.1, 31.9]; nominal $p < 0.01^b$)



Among pts in the pooled FAS and with a self-reported medical history of PsA, 124 were evaluable for efficacy. Among pts with a baseline DLQI score ≥ 1 , proportion differences and 95% CIs (using Miettinen-Nurminen method) were calculated adjusting for study, baseline weight category (≤ 90 kg, >90 kg), and geographic region (using Mantel-Haenszel test); *p*-values were based on Cochran-Mantel-Haenszel chi-square test stratified by study, baseline weight category (≤ 90 kg, >90 kg), and geographic region. CI=confidence interval; DLQI=Dermatology Life Quality Index; FAS=full analysis set; ICO=icotrokin; PBO=placebo, PsA=psoriatic arthritis, pts=participants, W=week.

ICO AE profile through W52 was consistent with that observed through W16				
Pooled Safety in Pts With PsO+PsA ^a	Through W16		Through W52	
	PBO (N=38)	ICO (N=88)	PBO→ICO ^b (N=30)	ICO (N=88)
Mean weeks/total PY of follow-up	14.8 / 10.8	15.7 / 26.5	33.6 / 19.3	48.8 / 82.4
Any AE	24 (63%)	47 (53%)	24 (80%)	72 (82%)
Incidence/100 PY (95% CI)	370 (213, 503)	273 (194, 350)	272 (159, 379)	221 (170, 272)
Serious AE	2 (5%)	1 (1%)	1 (3%)	4 (5%)
Incidence/100 PY (95% CI)	20 (<1, 76)	4 (0, 25)	5 (0, 34)	5 (2, 14)
Infection	12 (32%)	19 (22%)	12 (40%)	49 (56%)
Incidence/100 PY (95% CI)	139 (59, 222)	82 (45, 119)	82 (37, 139)	91 (65, 115)
Serious infection	1 (3%)	0	0	1 (1%)
Incidence/100 PY (95% CI)	10 (0, 62)	0 (0, 18)	0 (0, 27)	1 (0, 8)
Gastrointestinal AE	2 (5%)	7 (8%)	2 (7%)	12 (14%)
Incidence/100 PY (95% CI)	19 (0, 84)	28 (12, 58)	11 (<1, 42)	16 (9, 28)
Malignancy	1 (3%)	0	0	1 (1%)
Incidence/100 PY (95% CI)	10 (0, 62)	0 (0, 18)	0 (0, 27)	1 (0, 8)

Data shown are n (%), unless otherwise noted. Safety analysis set includes all randomized and treated pts. Incidence/100 PY: (number of pts with AEs/total PY at risk [time to first event]) × 100. CI based on study-size-adjusted Wald statistic. *Among pts in the pooled FAS and with a self-reported medical history of PsA. †Includes data after W16 for PsA in PsA-randomized pts who crossed over to receive ICQ. AEs=adverse event, CI=confidence interval, FAS=full-analysis set, ICQ=icatralin, PsA=placebo, PsO=psoriasis, pts=participants, PY=participant-years, W=week.