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Icotrokinra Demonstrated Superior Responses Compared With Placebo and Deucravacitinib in the Treatment of Moderate-to-Severe Plaque Psoriasis

Results Through Week 24 of the Phase 3 ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 Studies

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Conflicts of Interest

LSG: Served as an investigator, advisor and/or speaker for AbbVie, Amgen, Bristol Myers Squibb, Galderma, Johnson & Johnson, Lilly, Leo, Pfizer, Regeneron, Sanofi, Takeda.

AWA: Served as a research investigator, scientific advisor, or speaker for AbbVie, Amgen, Almirall, Arcutis, ASLAN, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, EPI, Incyte, Johnson & Johnson, Leo, Lilly, Novartis, Ortho, Pfizer, Regeneron, Sanofi, Sun, Takeda, and UCB.

RB: Served as an advisory board member, consultant, speaker and/or investigator for and received honoraria and/or grants from, AbbVie, Alumis, Amgen, AnaptysBio, Arcutis, BMS/Celgene, Dermavant, Eli Lilly, Johnson & Johnson, LEO Pharma, Nimbus, Takeda, UCB, VentyxBio, Vyne, Xencor, Zai Lab, and Zurabio; and is an employee and shareholder of Innovaderm Research.

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MS: Collaborated with the following companies: AbbVie, Affibody, Allergan, Almirall, Amgen, AstraZeneca, August Wolff, Boehringer Ingelheim, Bristol Myers Squibb, Dermapharm, Dermira, Incyte, Ipsen, Johnson & Johnson, LEO Pharma, Lilly, MedImmune, Menlo Therapeutics, Moonlake, MSD, Mundipharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Takeda, UCB Pharma.

MLG: Served as an investigator for Amgen, Boehringer Ingelheim, GSK, Johnson & Johnson, Lilly, Novartis, and Pfizer.

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MS: No conflicts of interest reported.

JR-M: Participated in clinical trials/received payments for presentations and consultancy/grants to assist with congresses from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Johnson & Johnson, Lilly, Leo Pharma, Novartis, and UCB.

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Background and Objective

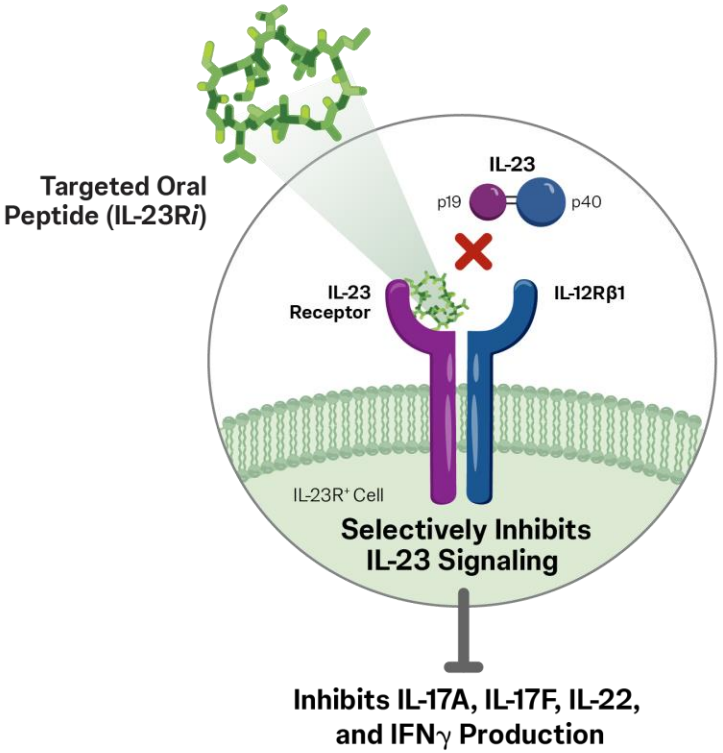
Icotrokinra for plaque psoriasis

- Patients with moderate-to-severe plaque psoriasis (PsO) are 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 significantly higher response rates vs placebo (PBO) at Week (W)16 in adults & adolescents with moderate-to-severe plaque PsO (ICONIC-LEAD) and in those with high-impact site PsO involving the scalp and genitals (ICONIC-TOTAL); no safety signals have been identified[2,3]

Objective

- Report key clinical and participant-reported outcomes (PROs) and safety findings from ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, the first PBO-controlled ICO trials to also include an active comparator arm vs deucravacitinib (Deucra)



[1]Fourie AM, et al. *Sci Rep*. 2024;14:17515. [2]Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA. [3]Gooderham M, et al. SID Annual Meeting; May 7-10, 2025; San Diego, CA, USA. **IFN**=interferon, **IL-12Rβ1**=interleukin-12 receptor beta 1, **IL-23R**=interleukin-23 receptor, **IL-23Ri**=interleukin-23 receptor inhibitor.

ICONIC-ADVANCE 1 & ICONIC-ADVANCE 2 – Study Design

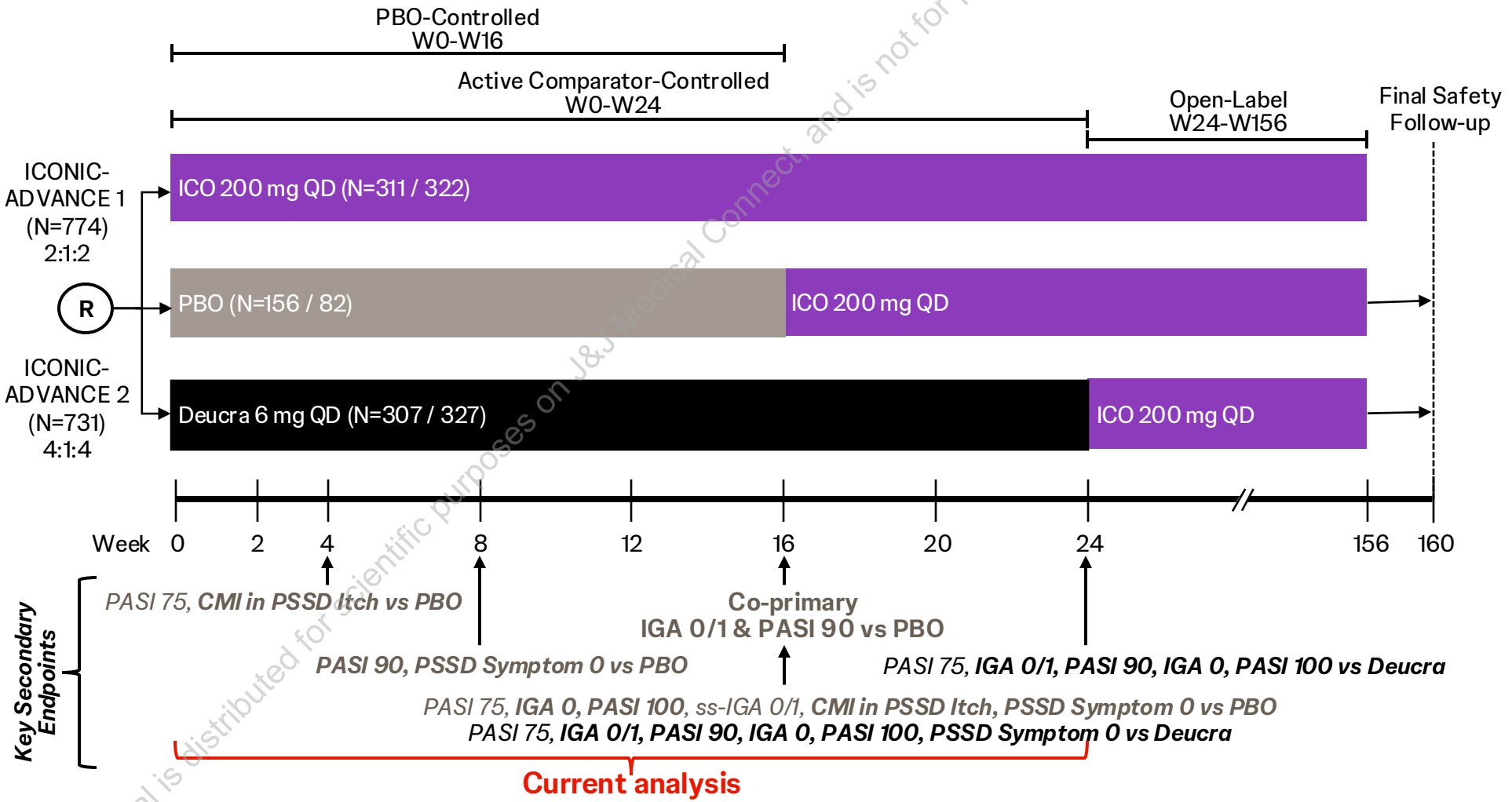
Moderate-to-severe plaque PsO

Key inclusion criteria

- ≥18 years
- Plaque PsO for ≥26 weeks
- BSA ≥10%; PASI score ≥12; IGA score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO
- Suitable candidate for Deucra per approved product labeling

Co-primary endpoints

- IGA score 0/1 & ≥2-grade improvement from baseline (IGA 0/1) vs PBO at W16
- PASI 90 vs PBO at W16



Bolded co-primary and key secondary endpoints presented in results. 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, **BSA**=body surface area, **CMI**=clinically meaningful improvement (≥4-point improvement from baseline), **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **PSSD**=Psoriasis Symptoms and Signs Diary, **QD**=once daily, **R**=randomization, **ss-IGA 0/1**=scalp-specific IGA score 0/1 & ≥2-grade improvement from baseline, **W**=week.

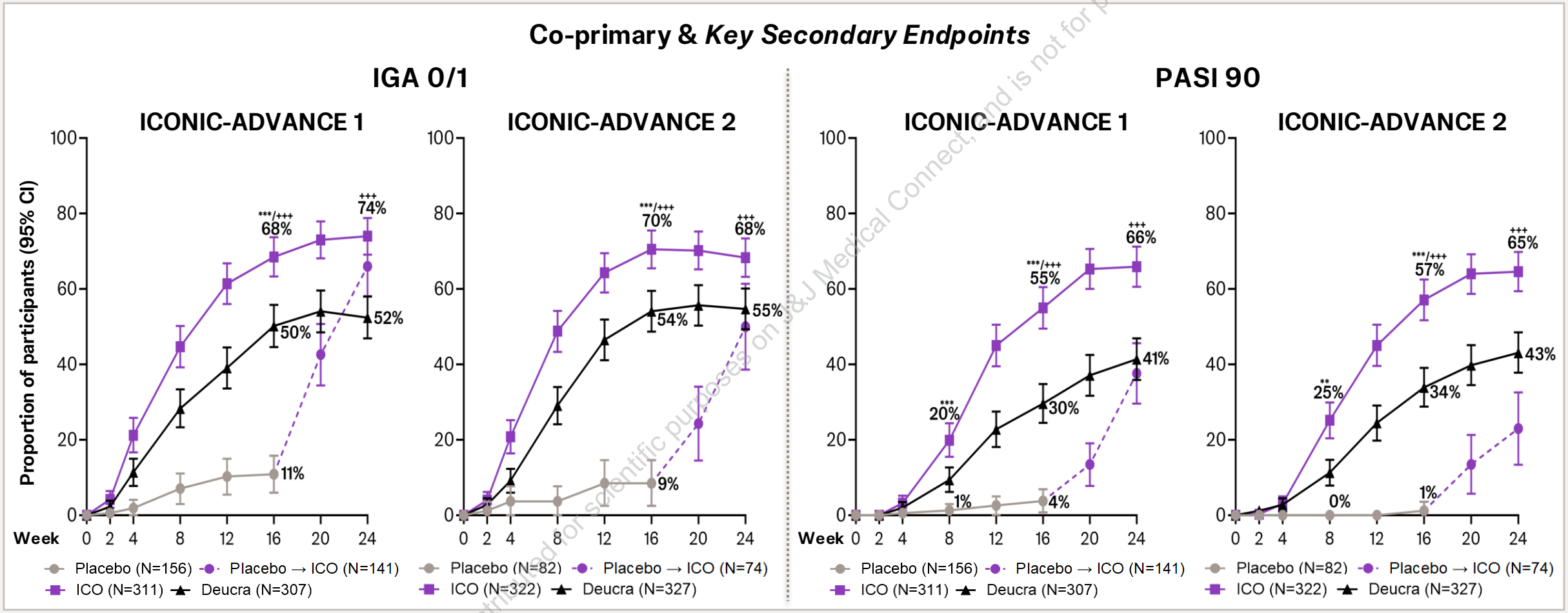
Baseline characteristics were generally comparable among treatment groups and across studies

Baseline Characteristics	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
	ICO (N=311)	PBO (N =156)	Deucra (N=307)	ICO (N=322)	PBO (N=82)	Deucra (N=327)
Demographics						
Age, yrs	47.1 (13.2)	46.9 (12.8)	46.3 (13.9)	45.9 (13.8)	48.4 (13.9)	45.6 (13.2)
Female	28%	33%	35%	32%	33%	32%
Asian/Black/White	22% / 1% / 74%	22% / 2% / 76%	25% / 1% / 72%	11% / 3% / 85%	18% / 2% / 79%	12% / 3% / 81%
BMI, kg/m^2	29.2 (6.3)	29.6 (8.1)	29.9 (7.3)	29.9 (6.4)	29.5 (5.8)	29.9 (6.9)[a]
Disease Characteristics						
PsO duration, yrs	17.5 (11.1)	17.9 (12.7)	16.8 (12.8)	17.4 (13.4)	21.2 (15.2)	16.8 (12.0)
% BSA with PsO	26.7 (15.8)	24.9 (14.8)	26.1 (15.8)	25.7 (13.9)	26.8 (15.1)	25.7 (14.4)
IGA score						
Moderate (3)	81%	79%	79%	78%	82%	82%
Severe (4)	19%	21%	21%	22%	18%	18%
PASI (0-72)	20.3 (6.9)	19.2 (6.6)	20.4 (7.9)	19.9 (7.0)	20.1 (7.5)	19.6 (6.6)
Prior PsO Treatments						
Phototherapy[b]	36%	34%	32%	30%	38%	33%
Systemic therapy[c]	76%	71%	73%	70%	71%	70%
Biologic therapy[d]	28%	27%	26%	24%	32%	24%

Overall, 94% of combined participants continued study treatment through W16 and W24

Data shown are mean (SD), unless otherwise noted. [a]Deucra: N=325. [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, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **UVB**=ultraviolet B, **W**=week.

ICO demonstrated significantly higher rates of IGA 0/1 and PASI 90 vs PBO at W16 (co-primary endpoints) & vs Deucra at W16 and W24

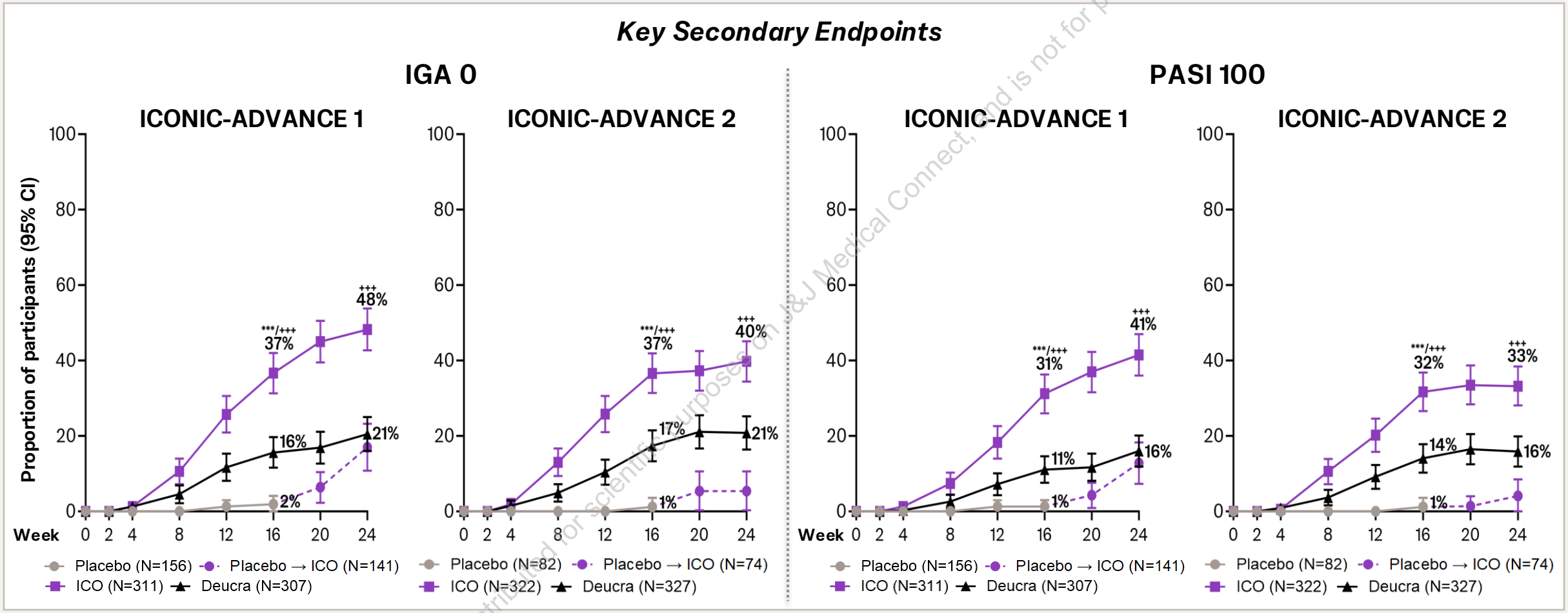


Multiplicity-adjusted **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO; multiplicity-adjusted ^{+}p<0.05, ^{++}p<0.01, ^{+++}p<0.001 vs Deucra

ICO showed early separation from PBO for achievement of PASI 90 at W8

P-values based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0/1**=IGA score 0/1 & ≥2-grade improvement from baseline, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

ICO demonstrated significantly higher rates of complete skin clearance vs PBO at W16 & vs Deucra at W16 and W24

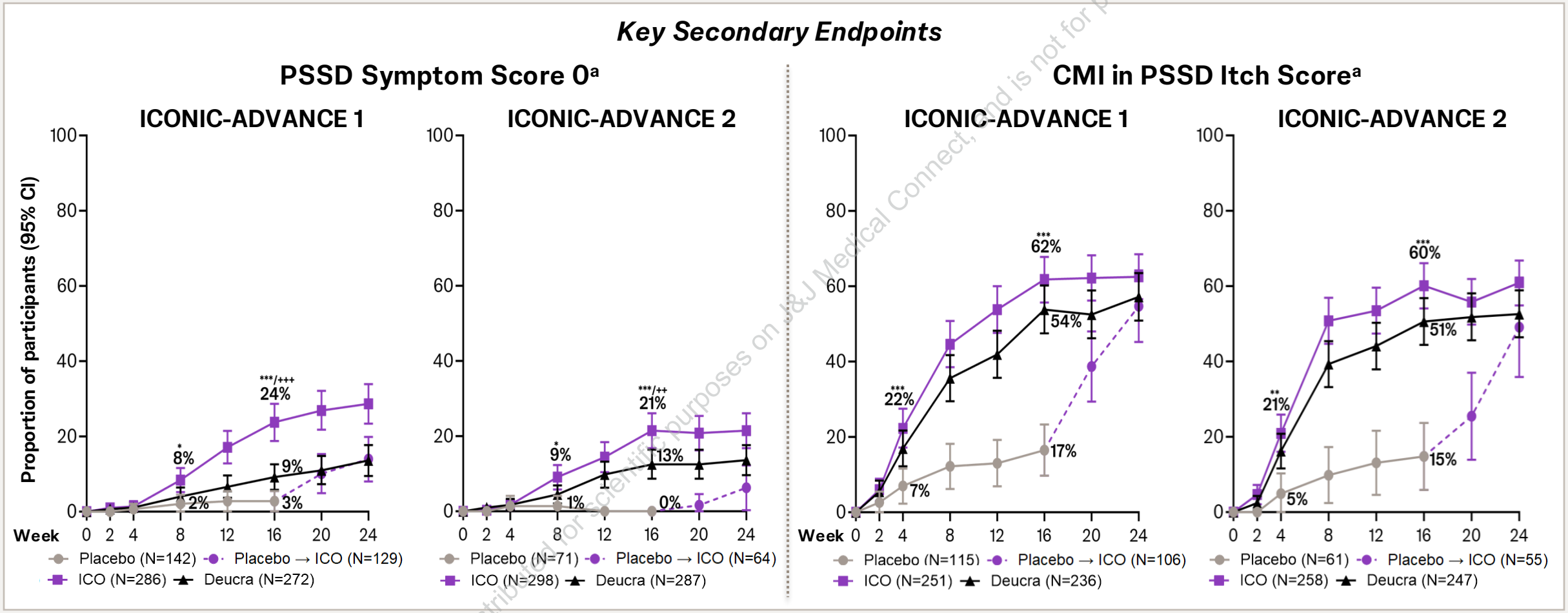


Multiplicity-adjusted **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO; multiplicity-adjusted ^{+}p<0.05, ^{++}p<0.01, ^{+++}p<0.001 vs Deucra

Rates of completely clear skin were ~2-fold or greater for ICO- vs Deucra-treated participants at W16 and W24

P-values based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

ICO demonstrated significantly higher rates of PsO symptom resolution vs PBO at W8 and W16 & vs Deucra at W16



Multiplicity-adjusted **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO; multiplicity-adjusted ^{+}p<0.05, ^{++}p<0.01, ^{+++}p<0.001 vs Deucra

Significantly higher proportions of ICO- vs PBO-treated pts reported meaningful improvement in PsO itch at W4 and W16

[a]Among participants (pts) with a baseline PSSD Symptom score >0 or PSSD Itch score ≥4. P-values based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. Fisher's exact test was used for PSSD Symptom score 0 at W8. **CI**=confidence interval, **CMI**=clinically meaningful improvement (≥4-point improvement from baseline), **Deucra**=deucravacitinib, **ICO**=icotrokinra, **PSSD**=Psoriasis Symptoms and Signs Diary, **PBO**=placebo, **W**=week.

ICO AE profile was similar to PBO through W16

Combined ICONIC-ADVANCE 1 & 2 AEs[a]	PBO-Controlled (W0-16)			Active Comparator-Controlled (W0-24)	
	PBO (N=237)	ICO (N=632)	Deucra (N=634)	ICO (N=632)	Deucra (N=634)
Mean weeks/total PY of follow-up	15.5 / 70.5	15.9 / 192.7	15.8 / 191.6	23.6 / 285.2	23.3 / 283.1
Any AE	136 (57%)	303 (48%)	360 (57%)	**359 (57%)**	**411 (65%)**
Incidence/100 PY (95% CI)[b]	**314 (254, 361)**	**225 (200, 251)**	300 (268, 330)	**201 (180, 221)**	**263 (237, 288)**
Serious AE	4 (2%)	14 (2%)	14 (2%)	18 (3%)	20 (3%)
Incidence/100 PY (95% CI)[b]	**6 (<1, 9)**	**7 (3, 11)**	7 (4, 11)	6 (3, 9)	7 (4, 10)
Serious infection[c]	1 (<1%)	1 (<1%)	4 (1%)	3 (<1%)	4 (1%)
Incidence/100 PY (95% CI)[b]	**1 (0, 9)**	**1 (0, 3)**	2 (1, 6)	1 (<1, 3)	1 (<1, 4)
Malignancy[d]	1 (<1%)	3 (<1%)	1 (<1%)	3 (<1%)	2 (<1%)
Incidence/100 PY (95% CI)[b]	**1 (0, 9)**	**2 (<1, 5)**	1 (0, 3)	1 (<1, 3)	1 (<1, 3)
AE leading to discontinuation	12 (5%)	13 (2%)	14 (2%)	15 (2%)	17 (3%)
Incidence/100 PY (95% CI)[b]	**17 (6, 24)**	**7 (3, 10)**	7 (4, 11)	5 (3, 8)	6 (3, 9)

Overall AE rates through W24 were lower with ICO than Deucra

Values are n (%) unless otherwise noted. [a]Safety analysis set included all randomized and treated participants (pts); ICONIC-ADVANCE 1 & 2: PBO=155/82, ICO=310/322, Deucra=307/327. [b]Incidence/100 PY: number of pts with AEs/total PY at risk × 100; CI based on study-size adjusted Wald statistics. [c]Included arthritis bacterial in the PBO group, infective exacerbation of chronic obstructive airways disease and pneumonia in the ICO group, and campylobacter colitis, lower respiratory tract infection, viral infection, and viral upper respiratory tract infection in the Deucra group. [d]Included invasive ductal breast carcinoma in the PBO group, pancreatic carcinoma and hepatic metastases, breast cancer, and keratoacanthoma in the ICO group,and buccal squamous cell carcinoma and malignant melanoma in situ in the Deucra group; all considered unrelated to study treatment by investigators. **AE**=adverse event, **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **PBO**=placebo, **PY**=participant-years, **W**=week.

No ICO safety signal was observed through W24

Combined ICONIC-ADVANCE 1 & 2 AEs[a]	PBO-Controlled (W0-16)			Active Comparator-Controlled (W0-24)	
	PBO (N=237)	ICO (N=632)	Deucra (N=634)	ICO (N=632)	Deucra (N=634)
Mean weeks/total PY of follow-up	15.5 / 70.5	15.9 / 192.7	15.8 / 191.6	23.6 / 285.2	23.3 / 283.1
Most common AEs (≥5%[b])					
Infection	73 (31%)	145 (23%)	202 (32%)	**190 (30%)**	**253 (40%)**
Incidence/100 PY (95% CI)[c]	128 (94, 151)	86 (72, 100)	130 (111, 147)	**80 (69, 92)**	**118 (104, 133)**
Nasopharyngitis	13 (5%)	37 (6%)	58 (9%)	56 (9%)	77 (12%)
Upper respiratory tract infection	8 (3%)	23 (4%)	33 (5%)	32 (5%)	49 (8%)
Headache	11 (5%)	26 (4%)	19 (3%)	28 (4%)	20 (3%)
Gastrointestinal AEs[d]	15 (6%)	45 (7%)	63 (10%)	55 (9%)	80 (13%)
Incidence/100 PY (95% CI)[c]	22 (12, 38)	24 (17, 32)	35 (26, 44)	20 (15, 26)	31 (24, 37)
Other AEs of Interest					
Acne[e]	0	4 (1%)	27 (4%)	5 (1%)	30 (5%)
Herpes[f]	6 (3%)	5 (1%)	13 (2%)	6 (1%)	18 (3%)

ICO infection rates were comparable to PBO through W16 & lower than with Deucra through W24

Values are n (%) unless otherwise noted. [a]Safety analysis set included all randomized and treated participants (pts); ICONIC-ADVANCE 1 & 2: PBO=155/82, ICO=310/322, Deucra=307/327. [b]Pts in any treatment group. [c]Incidence/100 PY: number of pts with AEs/total PY at risk × 100; CI based on study-size adjusted Wald statistics. [d]Based on gastrointestinal disorders SOC. [e]Included PTs acne, acne pustular, dermatitis acneiform. [f]Included PTs genital herpes simplex, herpes simplex, herpes virus infection, herpes zoster, oral herpes. **AE**=adverse event, **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **PBO**=placebo, **PT**=preferred term, **PY**=participant-years, **SOC**=system organ class, **W**=week.

Key Takeaways

In both pivotal Phase 3 ICONIC-ADVANCE 1 & 2 studies, adults with moderate-to-severe plaque PsO receiving icotrokinra (ICO) consistently demonstrated superior skin clearance and symptom relief vs PBO and Deucra:

ICO demonstrated significantly higher rates vs Deucra:

- Clear/almost clear skin
- Completely clear skin *(~2-fold or greater)*
- Symptom resolution

Favorable ICO safety:

- AE profile similar to PBO
- Overall AE & infection rates lower than Deucra
- No safety signal

ICO, a targeted oral peptide that binds and inhibits the IL-23R, has the potential to provide high rates of skin clearance and PsO symptom relief with a favorable safety profile in a once-daily pill

AE=adverse event, **Deucra**=deucravacitinib, **IL-23R**=interleukin-23 receptor, **PBO**=placebo, **PsO**=psoriasis.