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Maintenance of Response With Icotrokinra, a Targeted Oral Peptide, for the Treatment of Moderate-to-Severe Plaque Psoriasis

Randomized Treatment Withdrawal in Adults (Weeks 24-52) and Continuous Treatment in Adolescents (Through Week 52) From the Phase 3, ICONIC-LEAD Trial

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Conflicts of Interest

JS: Served as a speaker, consultant, advisory board member and/or investigator for AbbVie, Amgen, Arcutis, Aslan, Bristol Myers Squibb, Coval Biopharma, Dermavant, Eli Lilly, Johnson & Johnson, KoBio Labs, National Psoriasis Foundation, Novartis, Pfizer, Regeneron/Sanofi, and UCB.

YC: No conflicts of interest reported.

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.

MGL: Employee of Mount Sinai and receives research funds from: Abbvie, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, Clexio, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Johnson & Johnson, Pfizer, Sanofi-Regeneron, and UCB, and is a consultant for Aikium, Almirall, AltruBio Inc., Amgen, Apogee, Arcutis, Inc., AstraZeneca, Atomwise, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celltrion, CorEvitas, Dermavant Sciences, Dermsquared, Evommune, Inc., Facilitation of International Dermatology Education, Forte Biosciences, Galderma, Genentech, Incyte, LEO Pharma, Mayne Pharmaceuticals, Meiji Seika Pharma, Mindera, Mirium Pharmaceuticals, Oruka, Pfizer, Revolo, Sanofi-Regeneron, Seanergy, Strata, Sun Pharma, Takeda, Trevi, and Verrica.

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Background and Objective

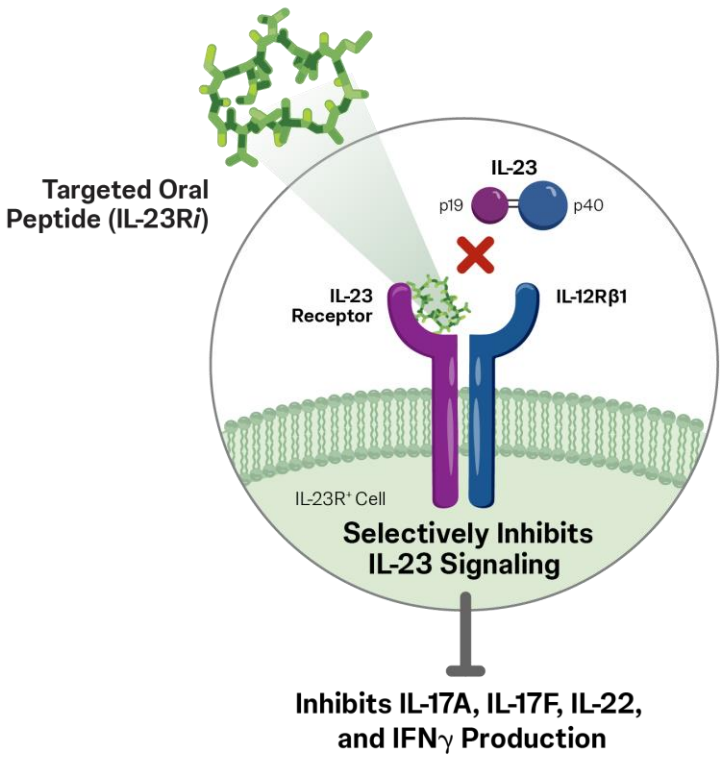
Icotrokinra for plaque psoriasis

- 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 rates of skin clearance vs placebo (PBO) at Week (W)16, with increasing response rates and no safety signal through W24 in adults & adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study[2]

Objective

- Report maintenance of ICO clinical response during the randomized-withdrawal period in adults (ICO vs PBO from W24-52), longer-term ICO effects in adolescents (through W52), and safety through W52 of ICONIC-LEAD



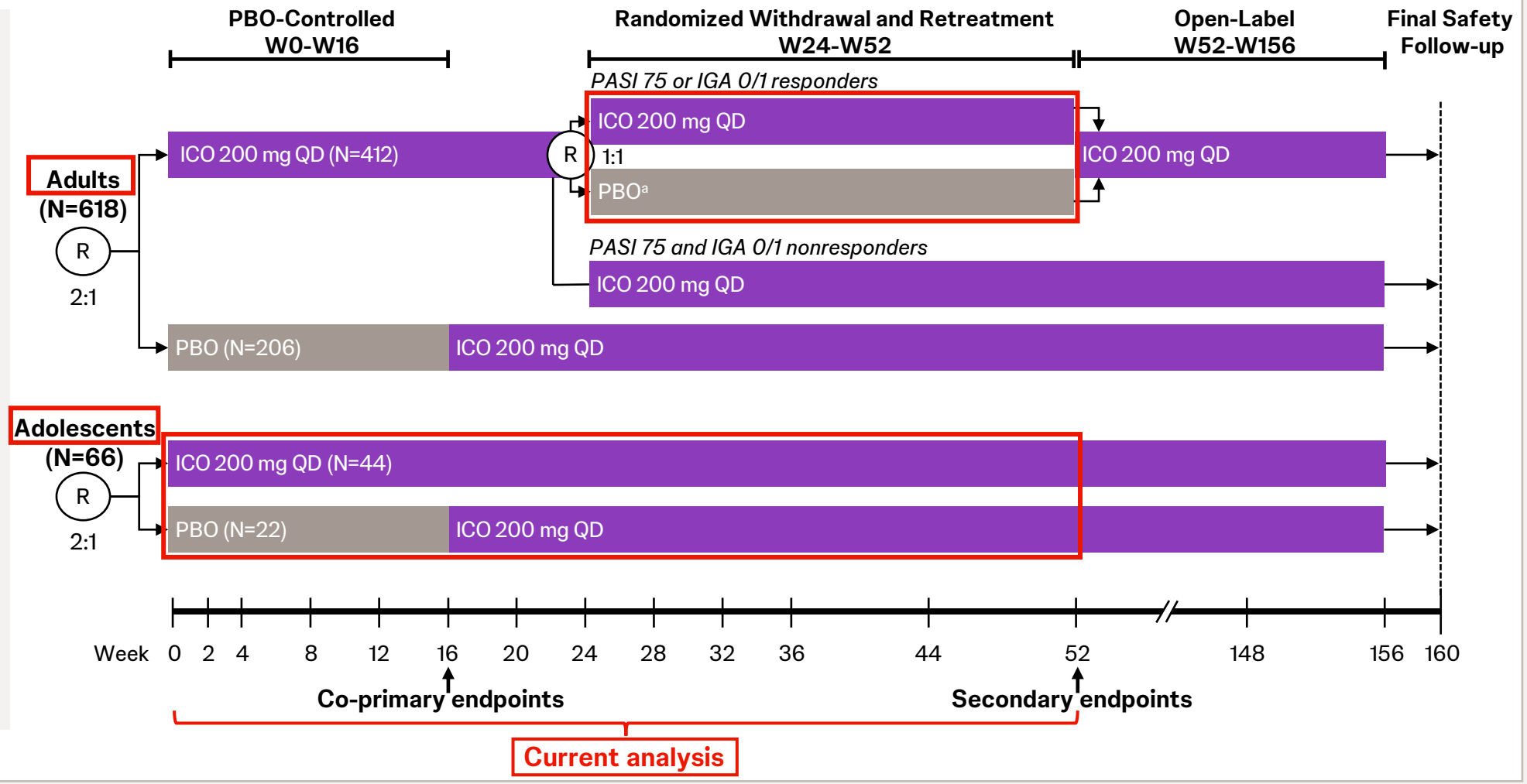
[1]Fourie AM, et al. *Sci Rep*. 2024;14:17515. [2]Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA. **IFN**=interferon, **IL-12Rβ1**=interleukin-12 receptor beta 1, **IL-23R**=interleukin-23 receptor, **IL-23Ri**=interleukin-23 receptor inhibitor.

ICONIC-LEAD – Study Design

Moderate-to-severe plaque PsO (N=684)

Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- BSA ≥10%
- PASI score ≥12
- IGA score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO



[a]Participants retreated with ICO upon loss of ≥50% PASI improvement observed at W24. **BSA**=body surface area, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **QD**=once daily, **W**=week.

Endpoints & Statistical Considerations

Adult W24 ICO Responders[a]: PASI & IGA Responses From W24 Through W52

- **Key Secondary Endpoints[b]**
  - **Response rates at W52[c]**
    - PASI 75 among PASI 75 responders at W24
    - PASI 90 among PASI 90 responders at W24
  - **Time to loss of response (LOR) through W52[c]**
    - Loss of PASI 75 among PASI 75 responders at W24
    - Loss of PASI 90 among PASI 90 responders at W24
- **Other Secondary Endpoints**
  - **Response rates at W52[c]**
    - IGA 0/1 & ≥2-grade-improvement from baseline among IGA 0/1 responders at W24
  - **Time to LOR through W52[c]**
    - Time to loss of IGA 0/1 among IGA 0/1 responders at W24

Adolescents: PASI & IGA Responses Through W52[c]

- PASI 75
- PASI 90
- IGA 0/1 & ≥2-grade-improvement from baseline

[a]Adults randomized to ICO at baseline who were PASI 75 or IGA 0/1 responders at W24; [b]Multiplicity-adjusted p-values for ICO vs PBO at/through W52; [c]Participants (pts) considered nonresponders or to have LOR: discontinued study drug due to a lack of efficacy or AE of worsening PsO; initiated a prohibited medication that could impact PsO; or met retreatment criterion for pts randomized to PBO at W24. For binary endpoints, nonresponder imputation was used for missing data (not imputed for LOR). **AE**=adverse event, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

Baseline characteristics were generally comparable across re-randomized treatment groups

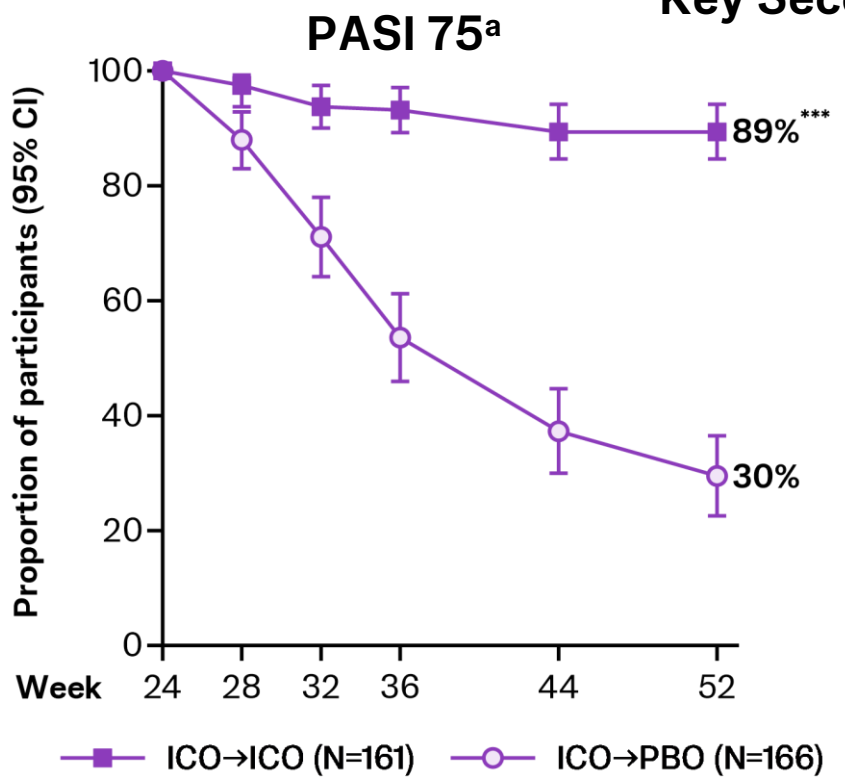
Baseline Characteristics: Adult W24 ICO Responders*	ICO → ICO (N=169)	ICO → PBO (N=172)
Demographics		
Age, yrs	46.5 (14.4)	44.5 (14.4)
Female	30%	38%
Race, Asian/Black/White	23% / 1% / 74%	24% / 1% / 73%
BMI, kg/m^2	29.0 (6.8)	29.7 (6.7)
Disease Characteristics		
PsO disease duration, yrs	19.2 (14.1)	18.6 (13.9)
% BSA with PsO	24.8 (14.0)	24.9 (14.7)
IGA score		
Moderate (3)	74%	78%
Severe (4)	26%	22%
PASI (0-72)	19.6 (6.7)	19.2 (7.3)
Prior PsO Treatments		
Phototherapy (PUVA or UVB)	31%	31%
Systemic therapy[a]	76%	72%
Biologic therapy[b]	35%	33%

***Among 412 adults randomized to ICO at baseline, 341 (83%) were recorded as PASI 75 or IGA 0/1 responders at W24**

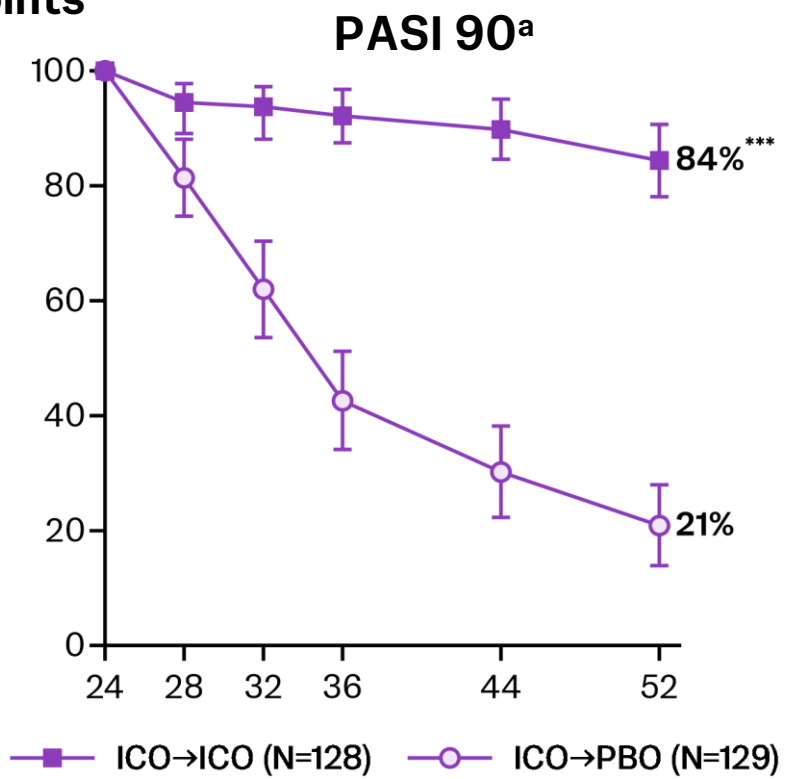
Data shown are mean (SD), unless otherwise noted. [a]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [b]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. **BMI**=body mass index, **BSA**=body surface area, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsO**=psoriasis, **PUVA**=psoralen plus ultraviolet A, **SD**=standard deviation, **UVB**=ultraviolet B, **W**=week.

W24 ICO responders re-randomized to ICO demonstrated superior maintenance of PASI response vs PBO at W52

Key Secondary Endpoints



Median time to LOR[a,b]
ICO→ICO: not reached* vs**
ICO→PBO: 16.9 weeks

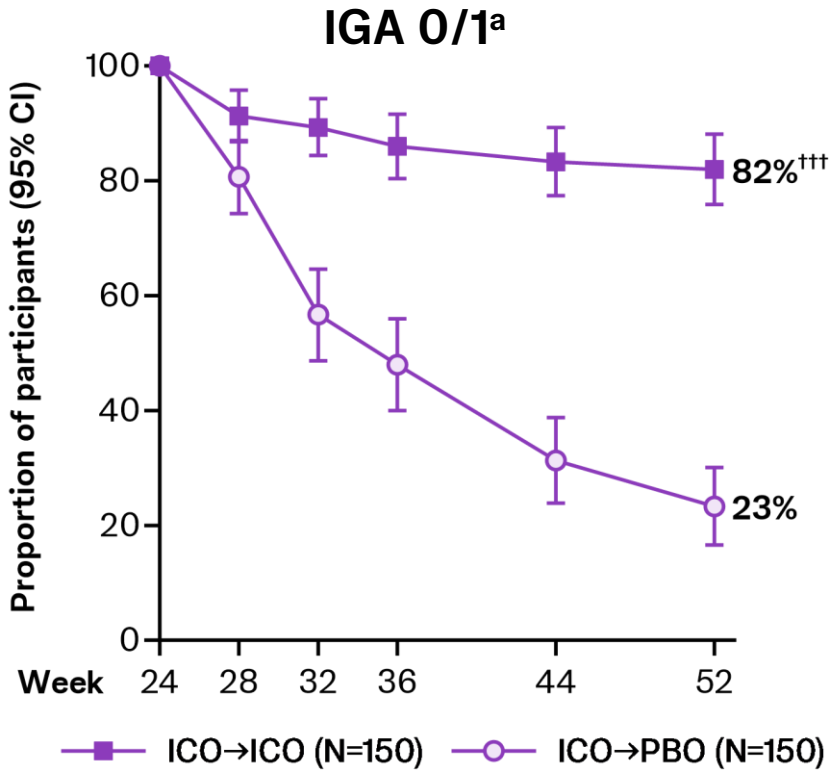


Median time to LOR[a,b]
ICO→ICO: not reached* vs**
ICO→PBO: 10.1 weeks

Multiplicity-adjusted ***$p<0.001$ vs PBO[c]

[a]Among W24 ICO PASI 75 and PASI 90 responders, respectively. [b]Based on life table method. [c]P-values for response rates (Cochran-Mantel-Haenszel chi-square test) and time to LOR (log-rank test) were stratified by geographic region (and for PASI 75, also stratified by PASI 90 response status at W24). **CI**=confidence interval, **ICO**=icotrokinra, **LOR**=loss of response, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

W24 ICO responders re-randomized to ICO demonstrated greater maintenance of IGA 0/1 response vs PBO at W52

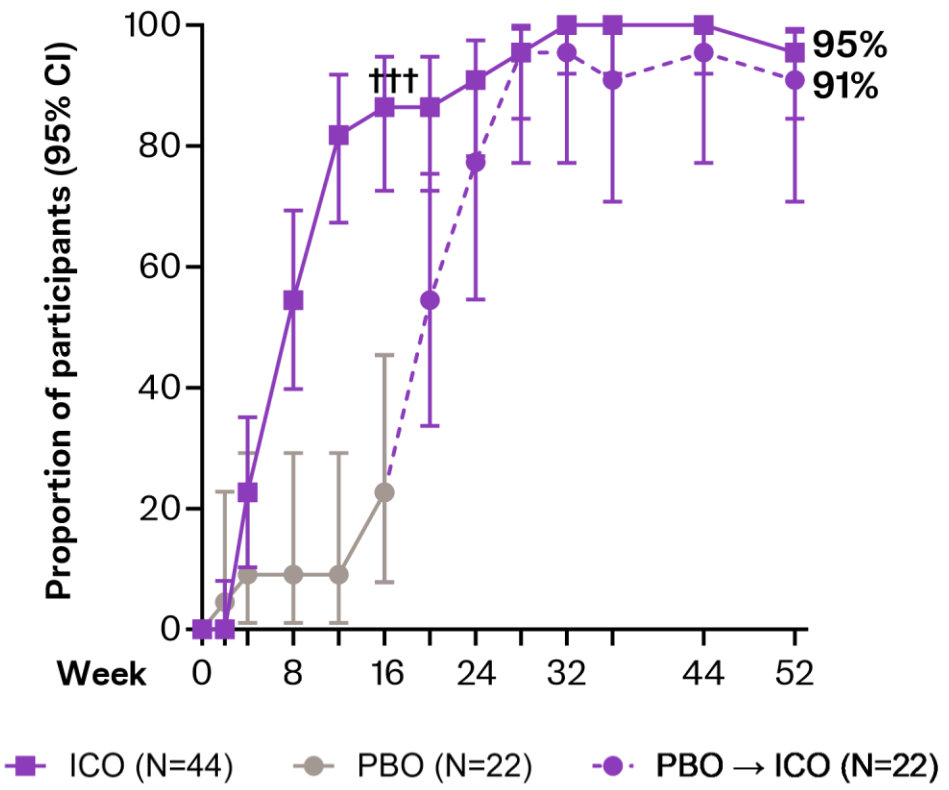


Median time to LOR[a,b]
ICO→ICO: not reached††† vs
ICO→PBO: 10.1 weeks

Nominal †††$p<0.001$ vs PBO[c]

[a]Among W24 ICO IGA 0/1 responders. [b]Based on life table method. [c]P-values for response rates (Cochran-Mantel-Haenszel chi-square test) and time to LOR (log-rank test) were stratified by geographic region and PASI 90 response status at W24. **CI**=confidence interval, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0/1**=IGA score 0/1 & ≥2-grade improvement from baseline, **LOR**=loss of response, **PBO**=placebo, **W**=week.

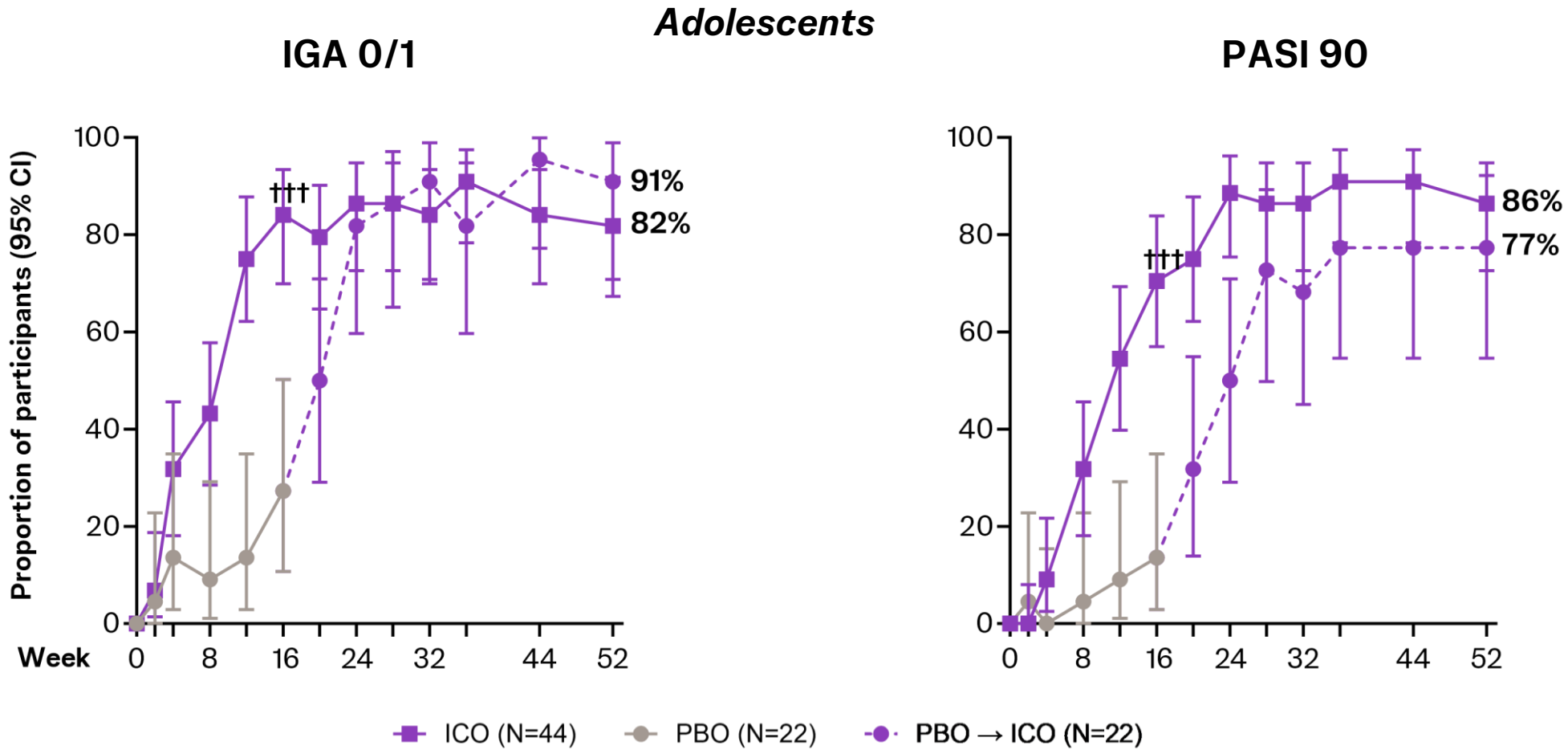
Adolescents: All (100%) ICO-randomized adolescents achieved PASI 75 by W32, with response rates maintained through W52



Nominal †††p<0.001 vs PBO[a]

[a]P-value based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region. **CI**=confidence interval, **ICO**=icotrokinra, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

~90% of ICO-randomized *adolescents* achieved clear/almost clear skin by W24, with durable response rates through W52



Nominal †††p<0.001 vs PBO[a]

[a]P-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region. **CI**=confidence interval, **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 AE profile through W52 was consistent with that observed through W16

AEs Through W52	PBO-Controlled[1] (Adults & Adolescents)		Active Treatment (Adults & Adolescents)		ICO Responders Re-Randomized at W24 (Adults)	
	ICO (W0-16; N=456)	PBO (W0-16; N=228)	ICO[a] (W16-52; N=213)	ICO (W0-52; N=456)	ICO → ICO (W24-52; N=168)	ICO → PBO[b] (W24-52; N=172)
Mean weeks of follow-up	15.9	15.8	35.3	43.4	27.7	27.8
Any AE	226 (50%)	112 (49%)	132 (62%)	313 (69%)	92 (55%)	82 (48%)
Most Common AEs						
Nasopharyngitis	31 (7%)	15 (7%)	23 (11%)	64 (14%)	21 (12%)	20 (12%)
Upper respiratory tract infection	30 (7%)	16 (7%)	24 (11%)	52 (11%)	9 (5%)	15 (9%)
SAE	6 (1%)	6 (3%)	4 (2%)	16 (4%)	3 (2%)	5 (3%)
Serious infection	1 (<1%)	0	1 (<1%)	1 (<1%)	0	1 (1%)
AE Leading to Discontinuation	6 (1%)	1 (<1%)	4 (2%)	10 (2%)	1 (1%)	3 (2%)
Gastrointestinal AE[c]	26 (6%)	13 (6%)	9 (4%)	51 (11%)	7 (4%)	8 (5%)
Active TB	0	0	0	0	0	0
Malignancy[d]	2 (<1%)	0	0	2 (<1%)	0	0

ICO AE profile in *adolescents* through W52 was consistent with that observed in the overall study population

[1]Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA. Safety analysis set included all randomized and treated participants (pts). [a]Includes data after W16 for PBO-randomized pts who crossed over to receive ICO. [b]Combined withdrawal and retreatment group. [c]Based on gastrointestinal disorders SOC. [d]Included adenocarcinoma of colon and prostate cancer.
AE=adverse event, **ICO**=icotrokinra, **PBO**=placebo, **SAE**=serious adverse event, **SOC**=system organ class, **TB**=tuberculosis, **W**=week.

Key Takeaways

In the pivotal phase 3 ICONIC-LEAD study evaluating the targeted oral peptide icotrokinra (ICO) through 1 year in adults & adolescents with moderate-to-severe plaque PsO:

Continuous ICO demonstrated superior maintenance of skin response among **adult** W24 ICO responders:

- *89% and 84% maintained PASI 75 and PASI 90, respectively, at W52*
- *LOR vs ICO withdrawal: Not reached vs 17 weeks (PASI 75) or 10 weeks (PASI 90)*

Continuous ICO demonstrated robust and durable skin clearance rates in ***adolescents*** through W52:

- *PASI 90: 86%*
- *PASI 75: 95%*
- *IGA 0/1: 82%*

- ICO AE profile through W52 was consistent with that observed through W16
- No ICO safety signal was identified through W52

AE=adverse event, **IGA**=Investigator's Global Assessment, **LOR**=loss of response, **PASI**=Psoriasis Area and Severity Index, **PsO**=psoriasis, **W**=week.