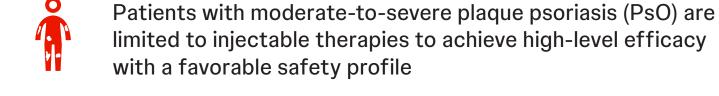
Maintenance of Response With Icotrokinra, a Targeted Oral Peptide, for the Treatment of Moderate-to-Severe Plaque Psoriasis: Randomized Treatment Withdrawal in Adults (Weeks 24-52) and Continuous Treatment in Adolescents (Through Week 52) From the Phase 3, ICONIC-LEAD Trial

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Background

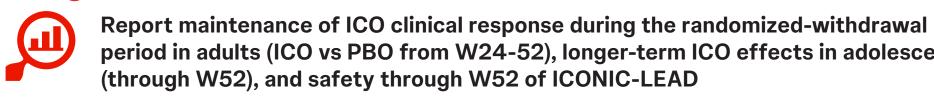


limited to injectable therapies to achieve high-level efficacy with a favorable safety profile Icotrokinra (ICO), a first-in-class targeted oral peptide:

 Precisely binds the interleukin-23 receptor (IL-23R) and inhibits IL-23 pathway signaling¹

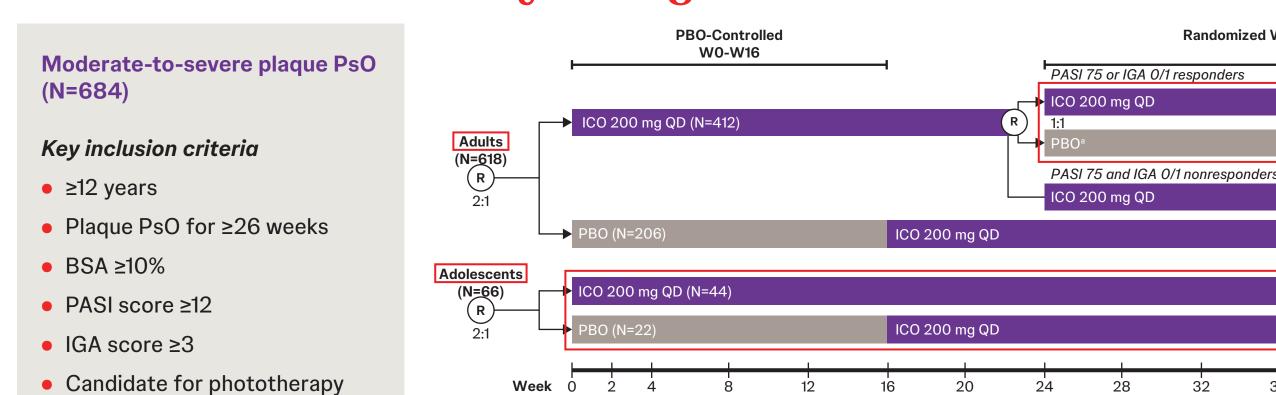
• Demonstrated significantly higher rates of skin clearance vs placebo (PBO) at Week (W)16, with increasing response rates and no safety signal through W24 in adults & adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study²





period in adults (ICO vs PBO from W24-52), longer-term ICO effects in adolescents (through W52), and safety through W52 of ICONIC-LEAD

ICONIC-LEAD – Study Design



plaque PsO



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

- Key Secondary Endpoints^b - Response rates at W52°
- PASI 75 among PASI 75 responders at W24
- PASI 90 among PASI 90 responders at W24
- Time to loss of response (LOR) through W52° Loss of PASI 75 among PASI 75 responders at W24

From Binding to its Receptor

Inhibits IL-17A, IL-17F, IL-22

- Loss of PASI 90 among PASI 90 responders at W24
- Other Secondary Endpoints

or systemic treatment for

- Response rates at W52°
- IGA 0/1 & ≥2-grade improvement from baseline among IGA 0/1 responders at W24
- Time to LOR through W52°
- Time to loss of IGA 0/1 among IGA 0/1 responders at W24

s andomized to ICO at baseline who were PASI 75 or IGA 0/1 responders at W24; Multiplicity-adjusted p-values for LOR). AE-adverse event.

Adolescents: PASI & IGA Responses Through W52° • PASI 75 • PASI 90 • IGA 0/1 & ≥2-grade improvement from baseline

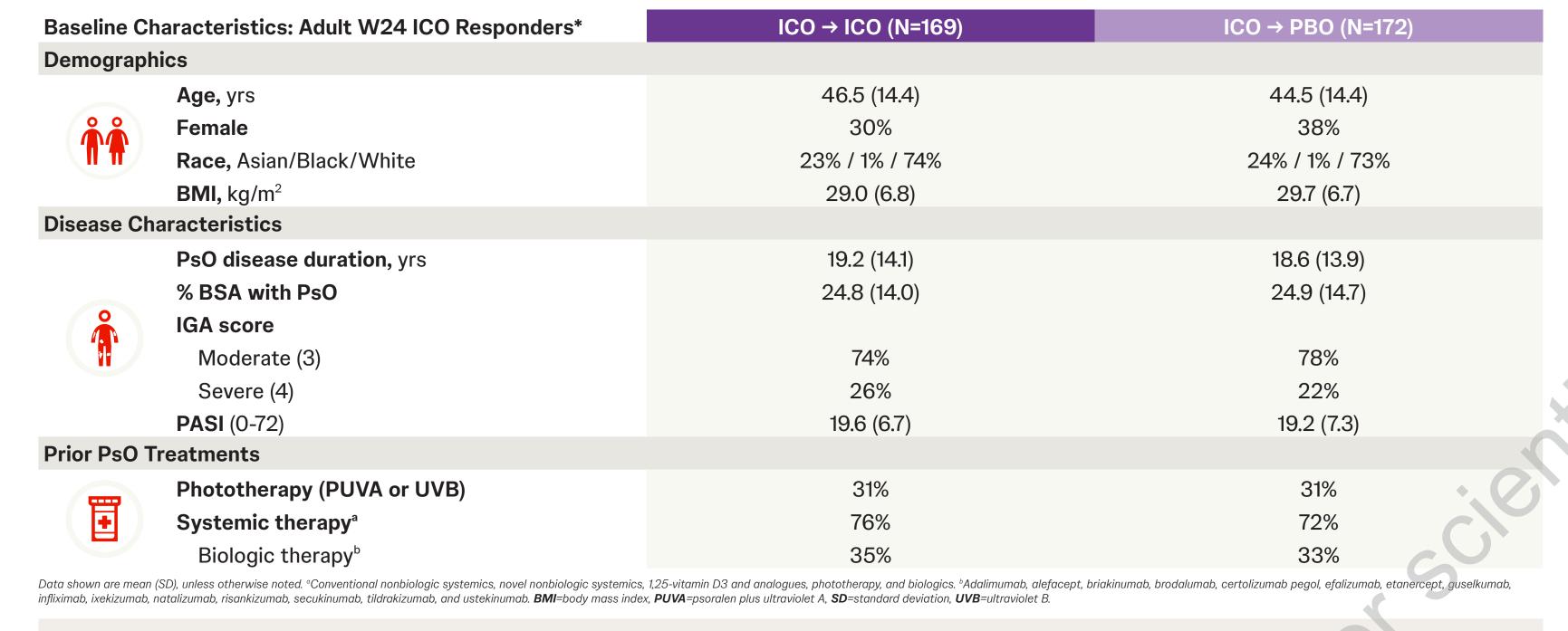
W52-W156

CO 200 mg QD

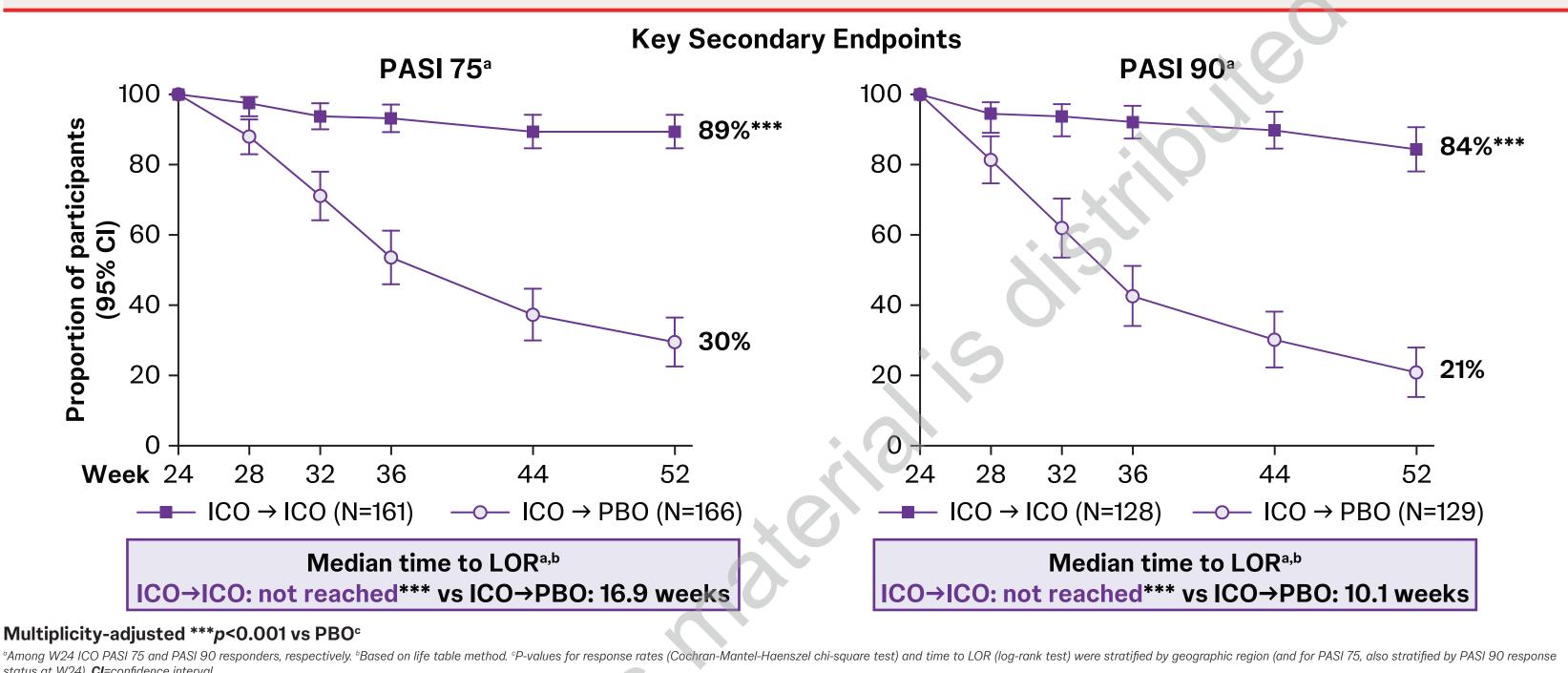
Results

Baseline characteristics were generally comparable across re-randomized treatment groups

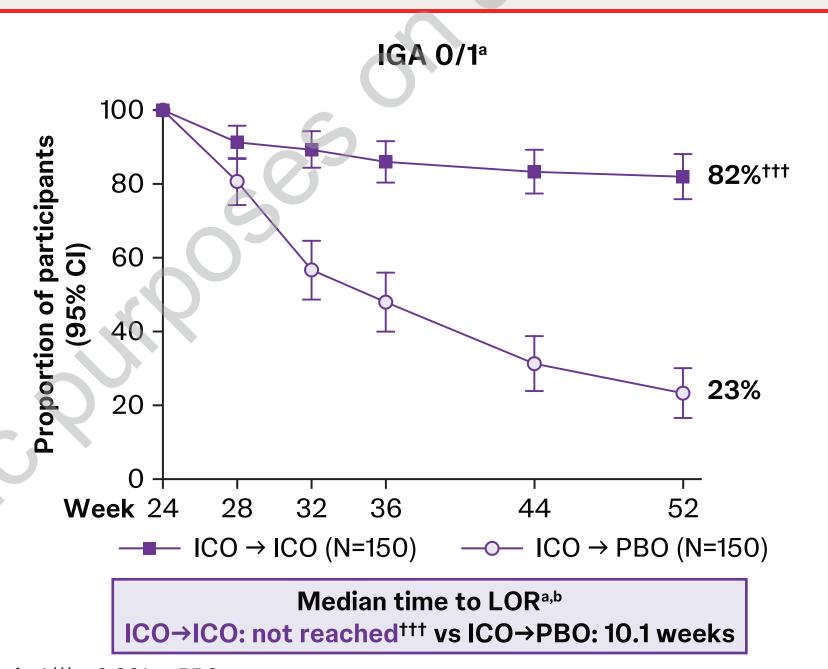
• *Among 412 adults randomized to ICO at baseline, 341 (83%) were recorded as PASI 75 or IGA 0/1 responders at W24



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

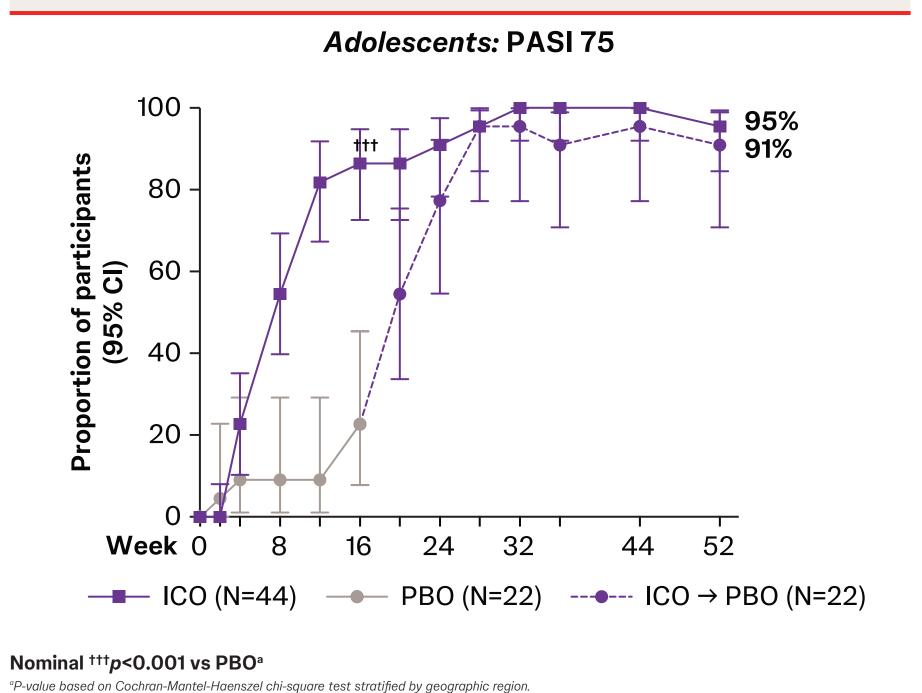


W24 ICO responders re-randomized to ICO demonstrated greater maintenance of IGA 0/1 response vs PBO at W52



"Among W24 ICO IGA 0/1 responders." Based on life table method. "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. **IGA 0/1**=IGA score 0/1 & ≥2-grade improvement from baseline.

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



Key Takeaways

In the pivotal phase 3 ICONIC-LEAD study evaluating the targeted oral peptide ICO through 1 year in adults & adolescents with moderate-tosevere 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)



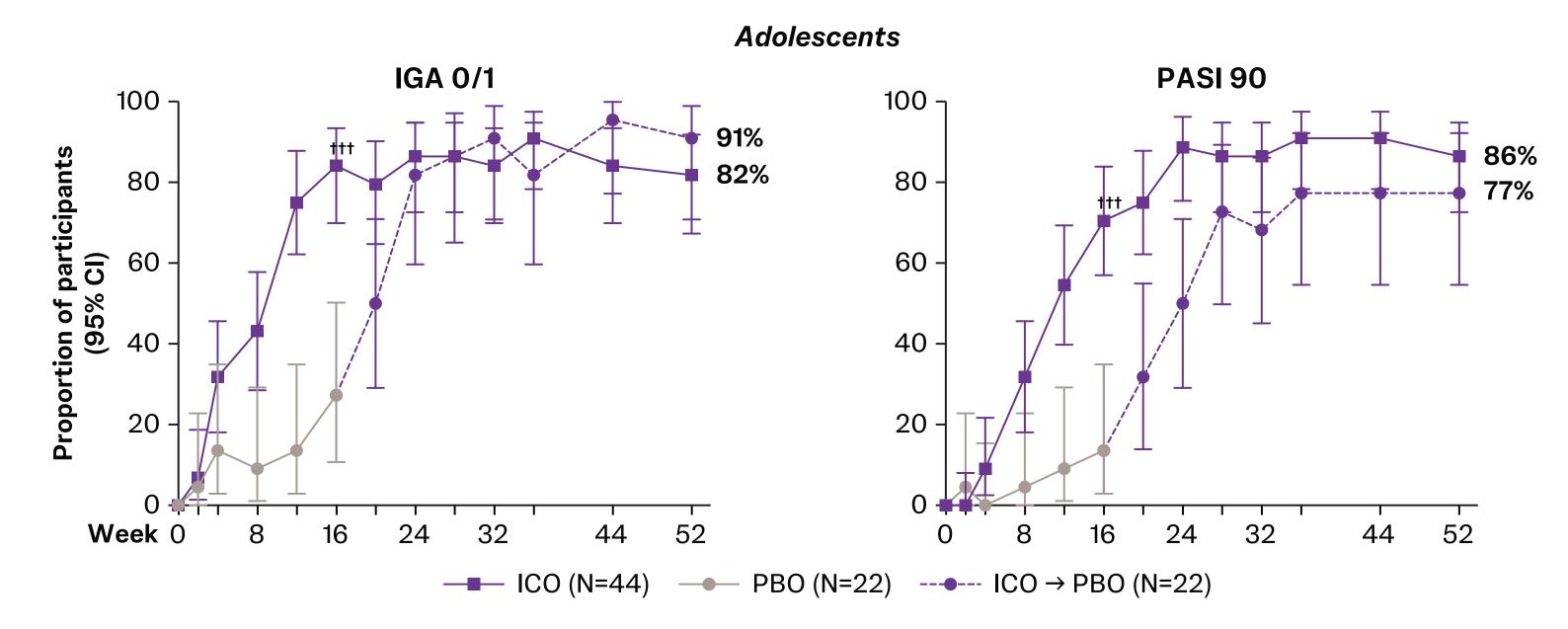
Continuous ICO demonstrated robust and durable skin clearance rates in adolescents through W52:

✓ 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

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



^aP-values based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region. IGA 0/1=IGA score 0/1 & ≥2-grade improvement from baseline.

ICO AE profile through W52 was consistent with that observed through W16

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

	PBO-Controlled ² (Adults & Adolescents)		Active Treatment (Adults & Adolescents)		ICO Responders Re-Randomized at W24 (Adults)	
AEs Through W52	ICO (W0-16; N=456)	PBO (W0-16; N=228)	ICO° (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

Safety analysis set included all randomized and treated participants. Includes data after W16 for PBO-randomized over to receive ICO. Combined withdrawal and retreatment group. Based on gastrointestinal disorders SOC. Included adenocarcinoma of colon and prostate cancer. SAE=serious adverse event, SOC=system organ class, TB=tuberculosis