Abstract N°: 1971

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&2 Studies

Linda Stein Gold*[1], April W. Armstrong[2], Robert Bissonnette[3], Nina Magnolo[4], Ronald Bernard Vender[5], Michael Sebastian[6], Maria Laura Galimberti[7], Athanasios Tsianakas[8], Marcelo Arnone[9], Paul Wallace[10], Margit Simon[11], José Riera Monroig[12], Bassey Edem[13], Jennifer Campbell[14], Ofelia Reyes-Servin[15], Lea Kephart[15], Yaung-Kaung Shen[15], Kellen Cresswell[15], Kim A. Papp[16]

[1]Henry Ford Health System, West Bloomfield, MI, United States
[2]Department of Dermatology, University of California Los Angeles, Los Angeles, CA, United States
[3]Innovaderm Research, Montreal, QC, Canada
[4]University Hospital Muenster, Muenster, Germany
[5]McMaster University and Dermatrials Research Inc., Hamilton, ON, Canada
[6]Dermatological Practice Dr. med. Michael Sebastian, Mahlow, Germany
[7]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
[8]Fachklinik Bad Bentheim, Bad Bentheim, Germany
[9]Hospital das Clínicas of University of São Paulo Medical School, São Paulo, Brazil
[10]Wallace Skin & Body Institute and Wallace Skin Research Center, Los Angeles, CA, United States
[11]Practice Dr. med. Margrit Simon, Berlin, Germany
[12]H. Clinic de Barcelona, Barcelona, Spain
[13]Johnson & Johnson, Leiden, Netherlands
[14]Johnson & Johnson, Cambridge, MA, United States
[15]Johnson & Johnson, Spring House, PA, United States
[16]Alliance Clinical Trials and Probity Medical Research, Waterloo, ON, Canada and Division of Dermatology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

Introduction & Objectives: Icotrokinra (ICO), a first-in-class targeted oral peptide, selectively binds the IL-23–receptor and inhibits IL-23 pathway signaling. In Phase 3 studies, ICO demonstrated significantly higher skin response rates and similar adverse event (AE) rates vs placebo (PBO) in adults and adolescents with moderate-to-severe plaque psoriasis (PsO; ICONIC-LEAD [NCT06095115]) and in plaque PsO involving high-impact sites (ICONIC-TOTAL [NCT06095102]).1,2 Here, the efficacy and safety of ICO vs PBO at Week (W)16 and ICO vs deucravacitinib (Deucra) at W16 and W24 in the first ICO active-comparator trials, ICONIC-ADVANCE (ADV) 1 & 2, are reported.

Materials & Methods: In these Phase 3, randomized, double-blind, PBO- and Deucra comparator-controlled studies, adults with moderate-to-severe plaque PsO (≥10% PsO body surface area; PASI ≥12; IGA score ≥3) were randomized (ADV-1, 2:1:2; ADV-2, 4:1:4) to once-daily (QD) oral ICO 200mg, PBO (PBO→ICO at W16), or Deucra 6mg through W24. Co-primary endpoints were IGA score of clear/almost clear (IGA0/1) and PASI90 for ICO vs PBO at W16. Key secondary endpoints, including ICO vs Deucra at W16/W24, were multiplicity-controlled. Analyses were performed using nonresponder imputation.

Results: ADV-1&2 randomized 774/731 participants (pts) to ICO (N=311/322), PBO (N=156/82), or Deucra (N=307/327). Co-primary endpoints were met: 68/70% of ICO- vs 11/9% of PBO-treated pts in ADV-1&2,

respectively, achieved IGA0/1; 55/57% vs 4/1% achieved PASI90 (all p<0.001). In both studies, ICO showed early separation from PBO for achievement of PASI90 (ADV-1&2 at W8: ICO 20/25% vs PBO 1/0%; both adjusted p<0.01; **Fig 1**) and demonstrated significantly higher rates of complete skin clearance vs PBO at W16 (ADV-1&2: IGA0 37/37% vs 2/1%; PASI100 31/32% vs 1/1%; all adjusted p<0.001; **Fig 2**).

ICO was also superior to Deucra, as shown by significantly higher proportions of ICO vs Deucra-treated pts achieving IGA0/1 (ADV-1&2: W16 68/70% vs 50/54%; W24 74/68% vs 52/55%) and PASI90 (ADV-1&2: W16 55/57% vs 30/34%; W24 66/65% vs 41/43%); all adjusted p<0.001 (**Fig 1**). Importantly, ICO demonstrated significantly higher rates of completely clear skin vs Deucra at W16 (ADV-1&2: IGA0 37/37% vs 16/17%; PASI100 31/32% vs 11/14%; all adjusted p<0.001). The differential effects of ICO vs Deucra on complete skin clearance (2-fold or greater rates at W16) were maintained through W24 (all adjusted p<0.001; **Fig 2**).

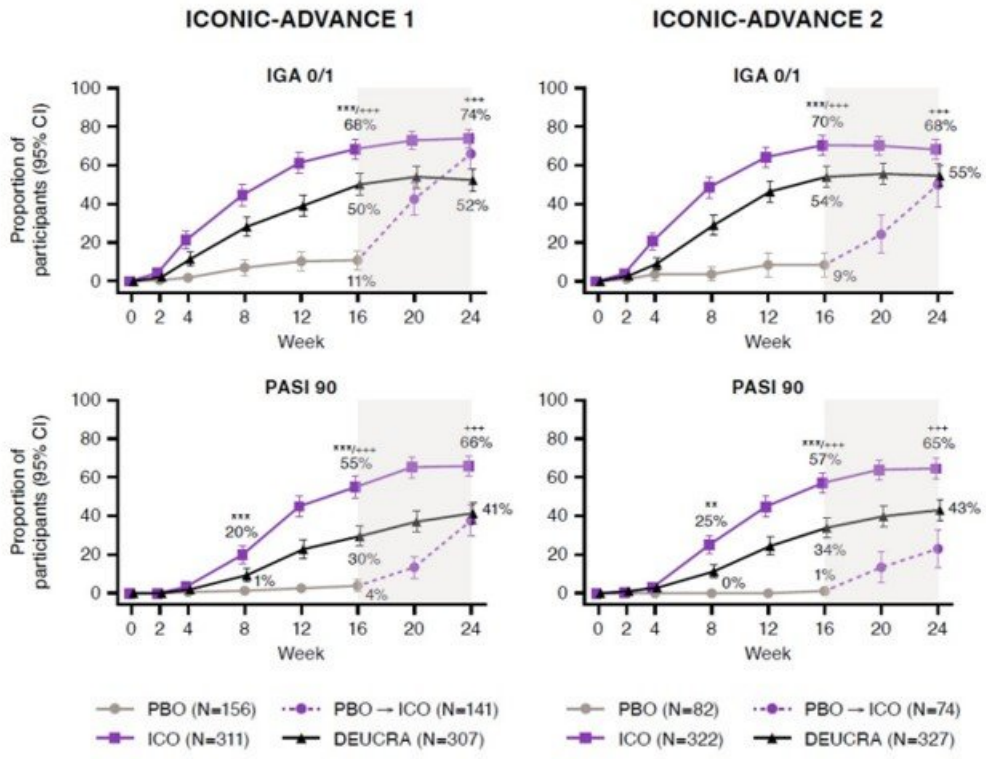
Proportions of pts with ≥1AE through W16 in ADV-1&2 were: ICO 46/49%, PBO 59/54%, and Deucra 56/57%. The most common system organ class was infections and infestations (ADV-1&2: ICO 21/25%, PBO 34/26%, Deucra 28/36%; the most commonly reported AEs were nasopharyngitis and upper respiratory tract infection). In the ICO group, AEs through W24 were consistent with W16.

Conclusion: In ICONIC-ADV 1&2, ICO showed superior skin responses vs PBO and Deucra. The AE profile of ICO was similar to PBO. ICO AE rates were numerically lower vs Deucra, primarily due to fewer pts with infections. Findings to date from Phase 3 ICO PsO trials suggest that this selective targeted oral peptide may provide high rates of skin clearance and favorable safety with QD oral dosing for adults and adolescents with moderate-to-severe plaque PsO.

1Bissonnette R. AAD; March 8, 2025; Orlando, FL.

2Gooderham M. SID; May 7-10, 2025; San Diego, CA.

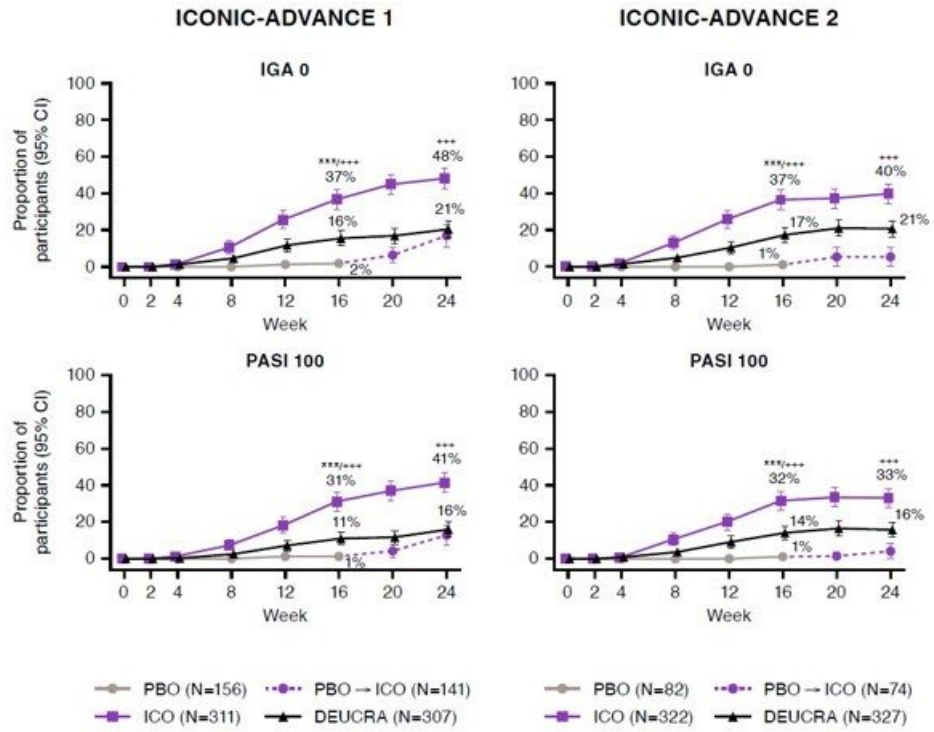
Figure 1. Proportions of Participants Achieving IGA0/1 and PASI90 Through W24



Adjusted */+, **/++, */+++p<0.05, <0.01, <0.001 vs PBO and Deucra, respectively.**

P-values were based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. Nonresponder imputation was assigned after pts discontinued study agent due to lack of efficacy or an adverse event of worsening of PsO, or initiated a prohibited PsO treatment. Observed data were used for pts who discontinued study agent for other reasons. After accounting for these intercurrent events, pts with missing data were considered as nonresponders.

Figure 2. Proportions of Participants Achieving IGA0 and PASI100 Through W24



Adjusted $^{*/+, **/++, ***/+++}$p<0.05, <0.01, <0.001 vs PBO and Deucra, respectively.

P-values were based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. Nonresponder imputation was assigned after pts discontinued study agent due to lack of efficacy or an adverse event of worsening of PsO, or initiated a prohibited PsO treatment. Observed data were used for pts who discontinued study agent for other reasons. After accounting for these intercurrent events, pts with missing data were considered as nonresponders.