Exposure - Response (ER) Relationships of Icotrokinra in Participants With Plaque Psoriasis: Phase 3 Results

Brinda Tammara[1], Emily Bozenhardt[1], Wangda Zhou[1], Cynthia DeKlotz[1], Paul Newbold[1], An Vermeulen[1], Mahesh Samtani[1]

[1]Johnson & Johnson, Spring House, PA, USA.

This presentation was sponsored by Johnson & Johnson.

Presented at: AAD Annual Meeting; March 27-31, 2026; Denver, Colorado, USA.

Disclosures

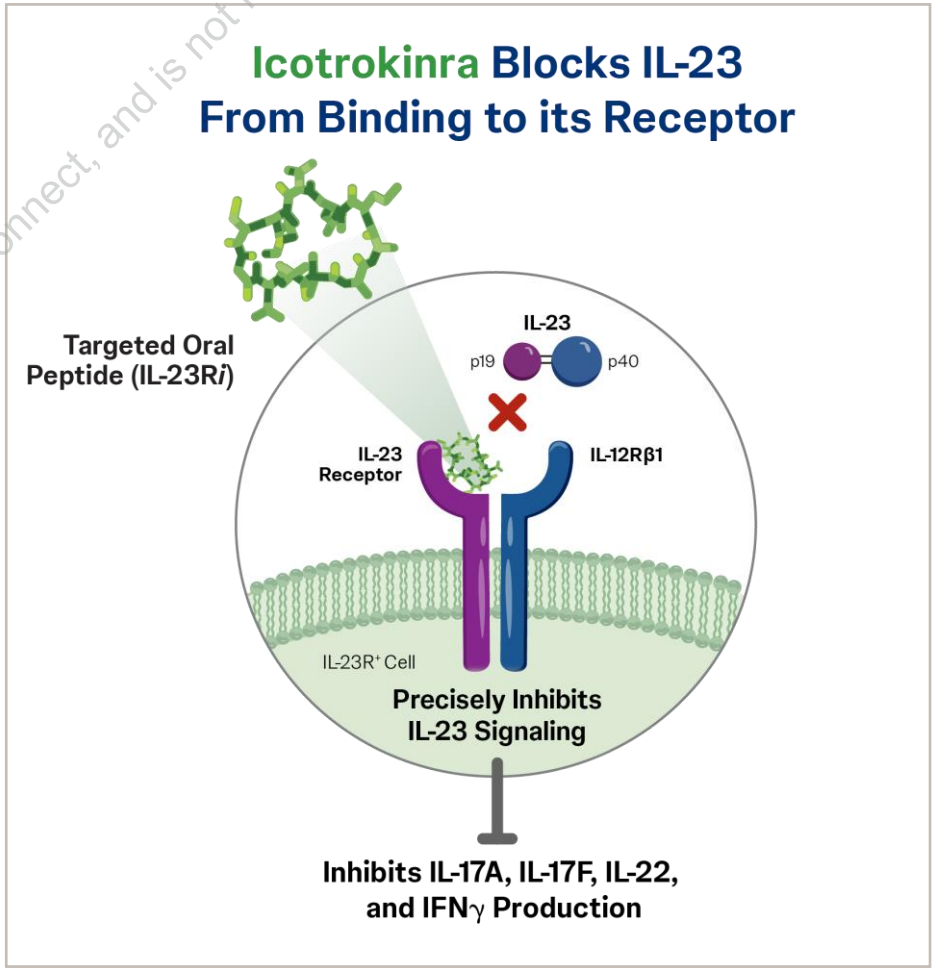
BT, EB, WZ, CD, PN, and AV: Employees of Johnson & Johnson; may own stock/stock options in Johnson & Johnson.
MS: Former Johnson & Johnson employee; may own stock/stock options in Johnson & Johnson.

Background

Plaque psoriasis (PsO) is a chronic inflammatory skin disease primarily driven by interleukin (IL)-23-mediated activation of the Th17 pathway, the upregulation of which is associated with proinflammatory cytokines and chemokines involved in disease pathogenesis[1]

Icotrokinra (ICO) is the first and only targeted oral peptide that precisely blocks the IL-23 receptor and inhibits IL-23 pathway signaling[2]

ICO demonstrated significantly higher rates of skin clearance and a favorable safety profile across 4 pivotal, Phase 3, randomized controlled trials (RCTs) in participants (pts) with plaque PsO[3-5]



IFN=interferon, **IL-12Rβ1**=IL-12R beta 1, **IL-23Ri**=IL-23R inhibitor.

Objective

Evaluate the studied ICO dose regimen across RCTs in pts with plaque PsO by characterizing the relationships between ICO systemic exposure and

- **Clinical response at Week (W) 16**
- **Adverse events (AEs) through W16**

Analyses

Population pharmacokinetic (PK) analyses

- Performed using integrated data (N=2,551) from healthy volunteers in Phase 1 studies and pts with moderate-to-severe plaque PsO in Phase 2 (oral ICO 25 mg QD, 25 mg BID, 50 mg QD, 100 mg QD, or 100 mg BID) and Phase 3 studies (oral ICO 200 mg QD)
- ICO PK profile was described with a 1-compartment model with first-order absorption and first-order elimination

Exposure-response (ER) analyses - Efficacy at W16

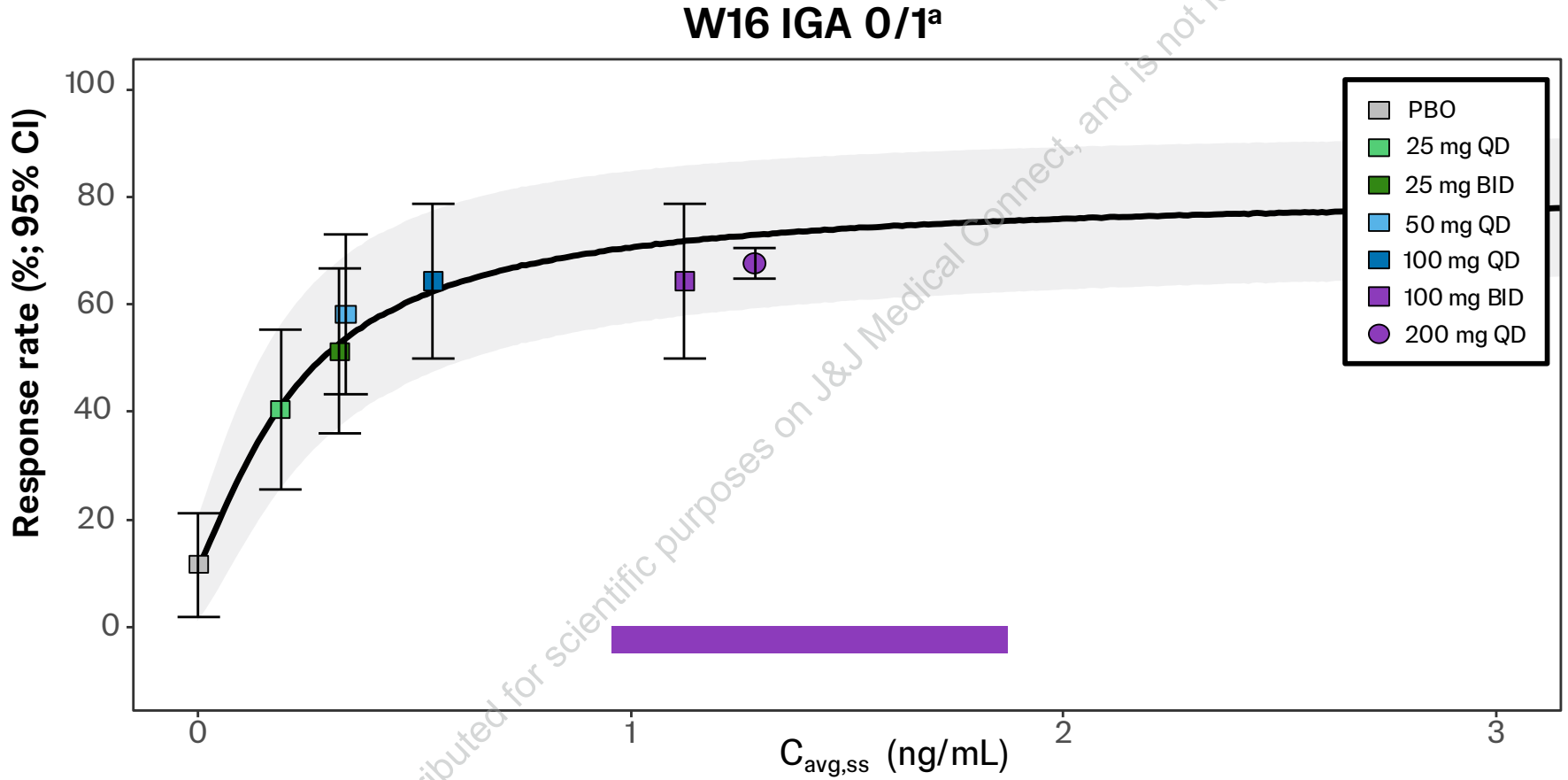
- W16 observed and model-predicted IGA/PASI response rates (from ordinal logistic E_{max} regression using Phase 2 data only) were plotted vs $C_{avg,ss}$ (from population PK analysis)
  - Observed data were pooled for Phase 2 (FRONTIER 1) and Phase 3 studies (ICONIC-LEAD, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2
- W16 observed PASI/IGA response rates were plotted vs quartiles of exposure (based on $C_{avg,ss}$)
  - Observed data were pooled for 3 Phase 3 studies (ICONIC-LEAD and ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2; N=1,553)
  - Observed data were presented separately for Phase 3 ICONIC-TOTAL (N=311)

ER analyses - Safety through W16

- Rates of pts experiencing AEs through W16 were plotted vs quartiles of exposure (based on $C_{avg,ss}$)
  - AE data pooled for 4 Phase 3 studies (ICONIC-LEAD, ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and ICONIC-TOTAL)

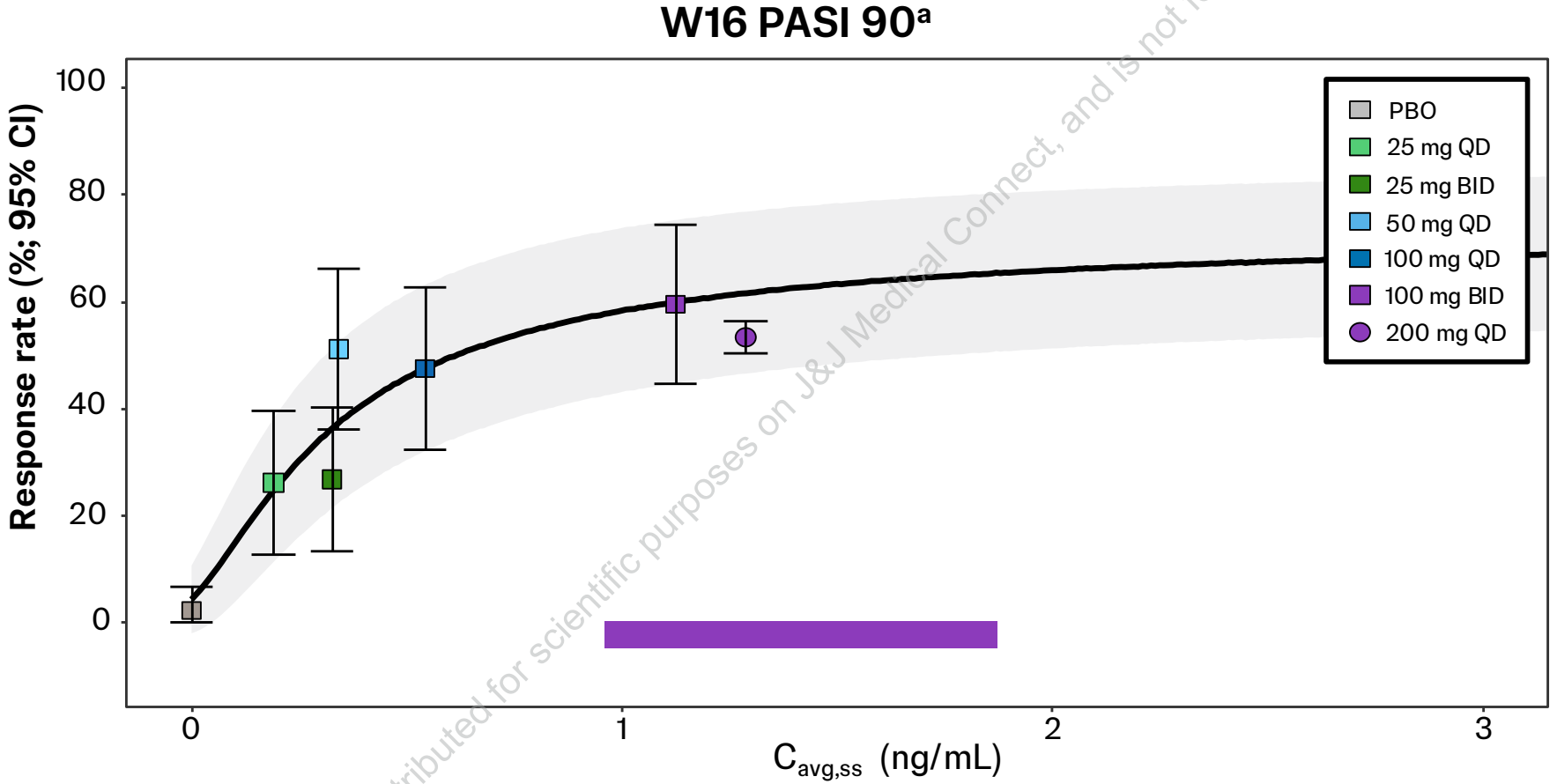
BID=twice daily, **BSA**=body surface area, **$C_{avg,ss}$**=post-hoc average study-state drug concentration, **E_{max}**=maximum effect, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index,[5] **QD**=once daily.

W16 ER analyses indicated ICO 200 mg QD achieved similar IGA 0/1 and PASI 90 response rates as 100 mg BID



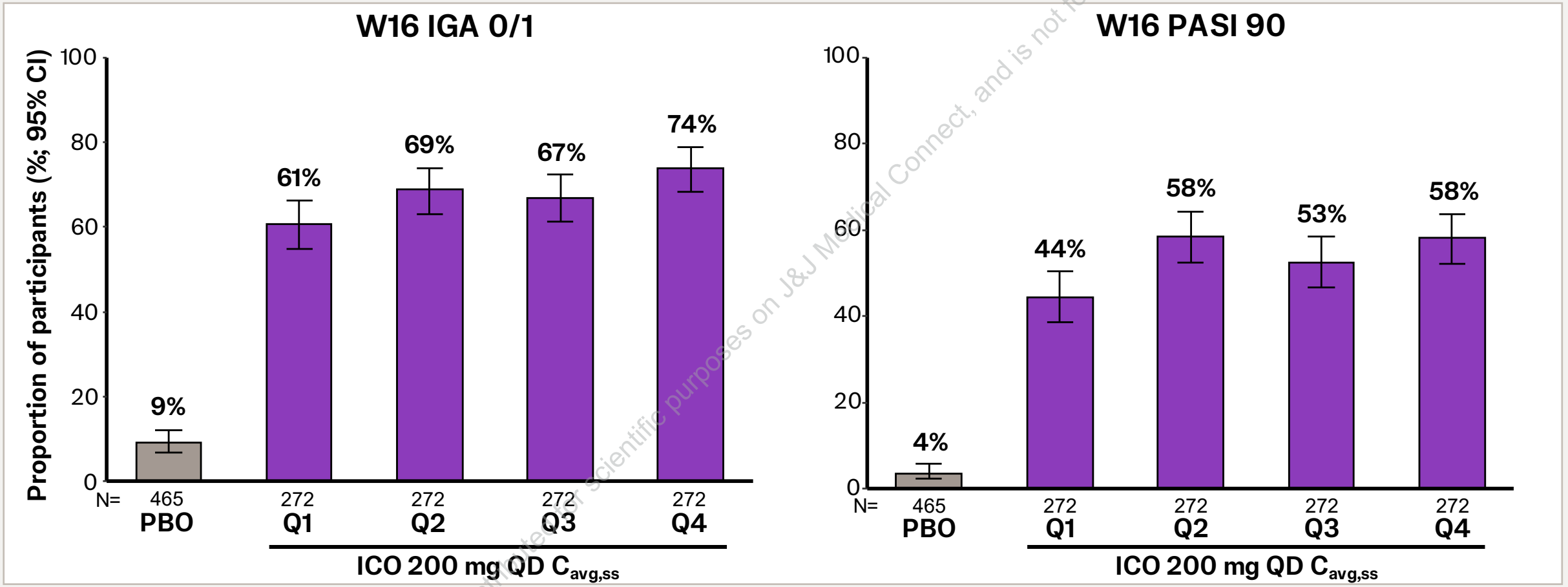
[a]Achievement of IGA score of 0 (clear) or 1 (almost clear) with ≥2 grade improvement from baseline. The black solid line represents the model-predicted response rate derived from ordinal logistic E_{max} regression based on FRONTIER 1. Grey shading represents 95% CI of model predicted response rate. Data points and whiskers correspond to the observed response rates and corresponding 95% CIs and includes data from FRONTIER 1, ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2. The horizontal-colored bar represents the 25th-75th percentile of PK post hoc exposure metrics of the 200 mg QD dosing regimen. **CI**=confidence interval, **PBO**=placebo.

W16 ER analyses indicated ICO 200 mg QD achieved similar IGA 0/1 and PASI 90 response rates as 100 mg BID



[a]Achievement of 90% or greater improvement from baseline in PASI score. The black solid line represents the model-predicted response rate derived from ordinal logistic E_{max} regression based on FRONTIER 1 . Grey shading represents 95% CI of model predicted response rate. Data points and whiskers correspond to the observed response rates and corresponding 95% CIs and includes data from FRONTIER 1, ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2. The horizontal-colored bar represents the 25th-75th percentile of PK post hoc exposure metrics of the 200 mg QD dosing regimen.

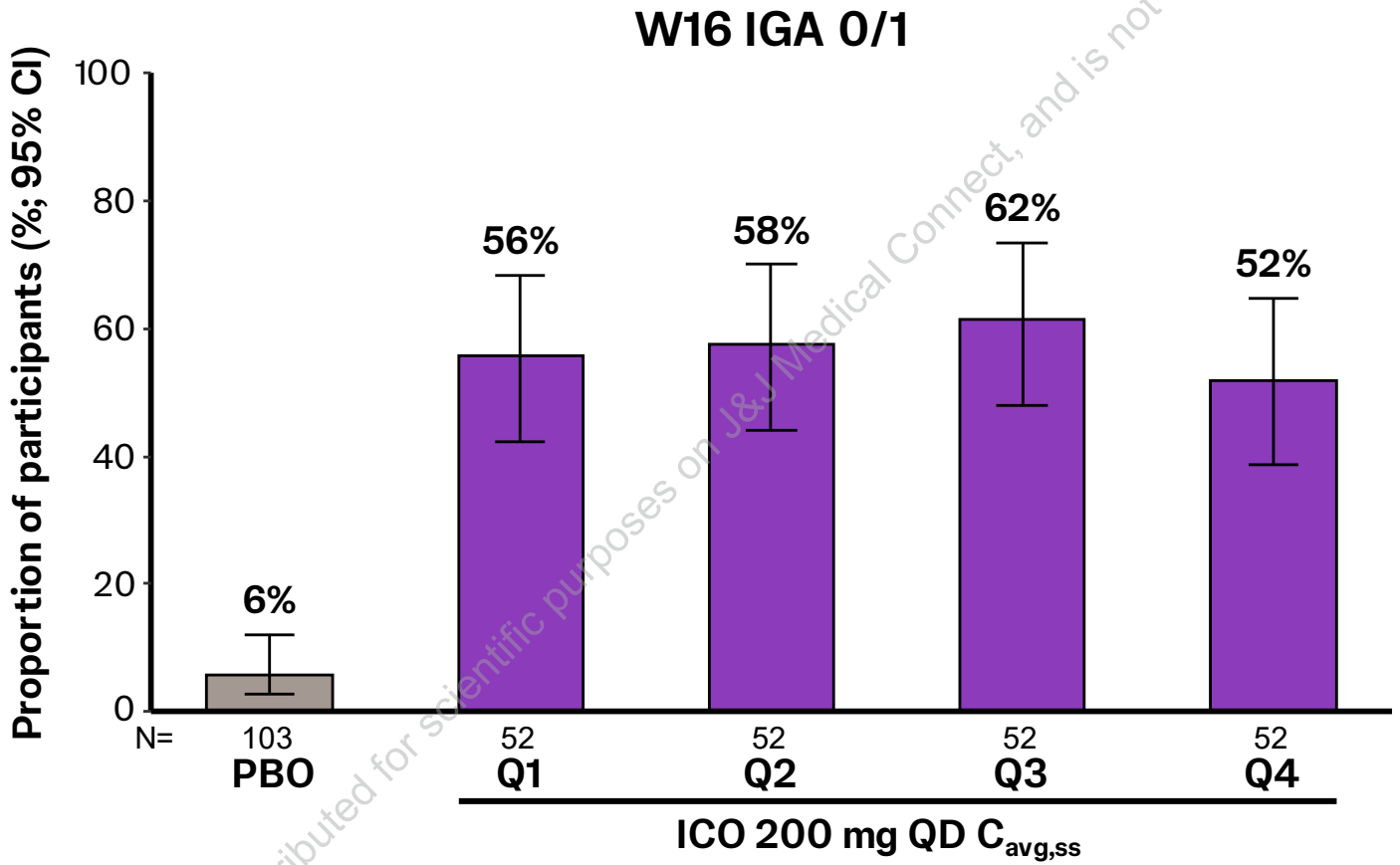
ICO 200 mg QD provided consistently high W16 IGA 0/1 and PASI 90 response rates across exposure quartiles in 3 pooled RCTs



- **ICO demonstrated higher W16 PASI 90 and IGA 0/1 response rates versus PBO across all exposure quartiles**
- **With increasing exposure, response rates were stnle and fell on the flat part of the ER curve**

Includes data from ICONIC-LEAD, ICONIC-ADVANCE 1, and ICONIC-ADVANCE 2. $C_{avg,ss}$ quartile ranges: Q1: 0.325 to 0.957 ng/mL, Q2: 0.960 to <1.29 ng/mL; Q3: 1.29 to <1.8727 ng/mL; Q4: 1.8728 to 17.0 ng/mL. **Q**=quartiles.

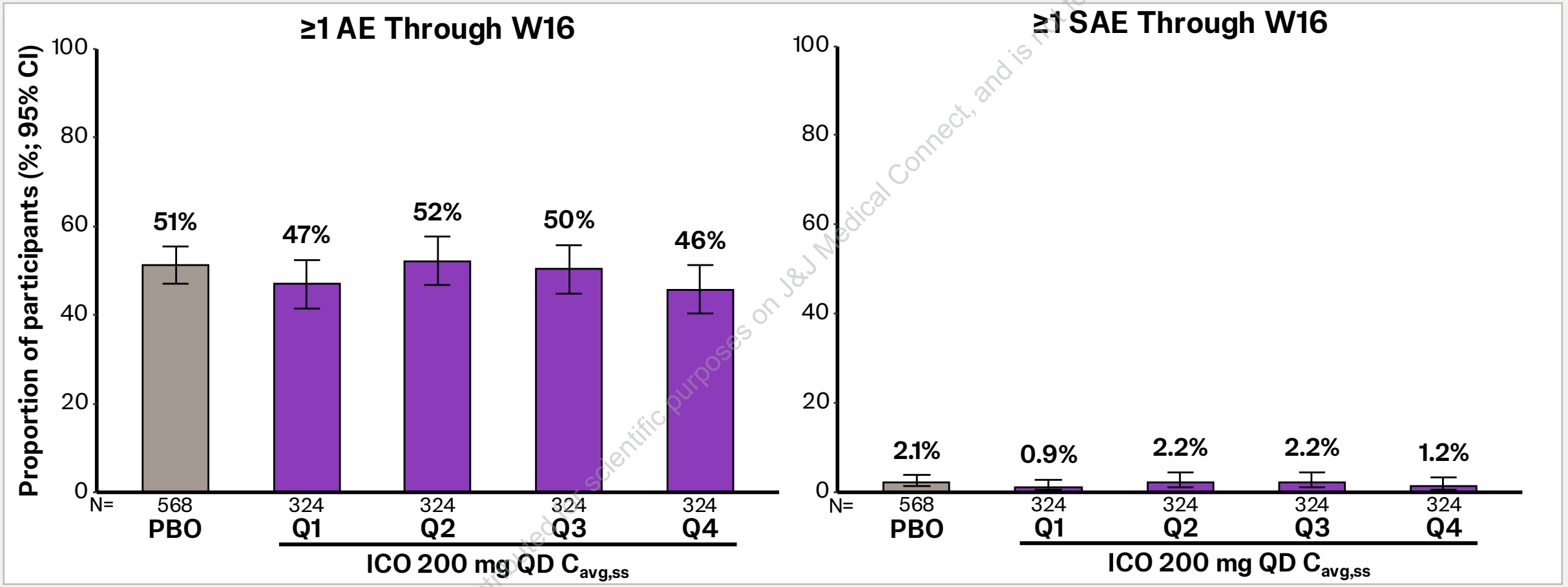
ICO 200 mg QD provided consistently high W16 IGA 0/1 response rates across exposure quartiles in ICONIC-TOTAL



ICO demonstrated higher W16 IGA 0/1 response rates compared with PBO across all exposure quartiles

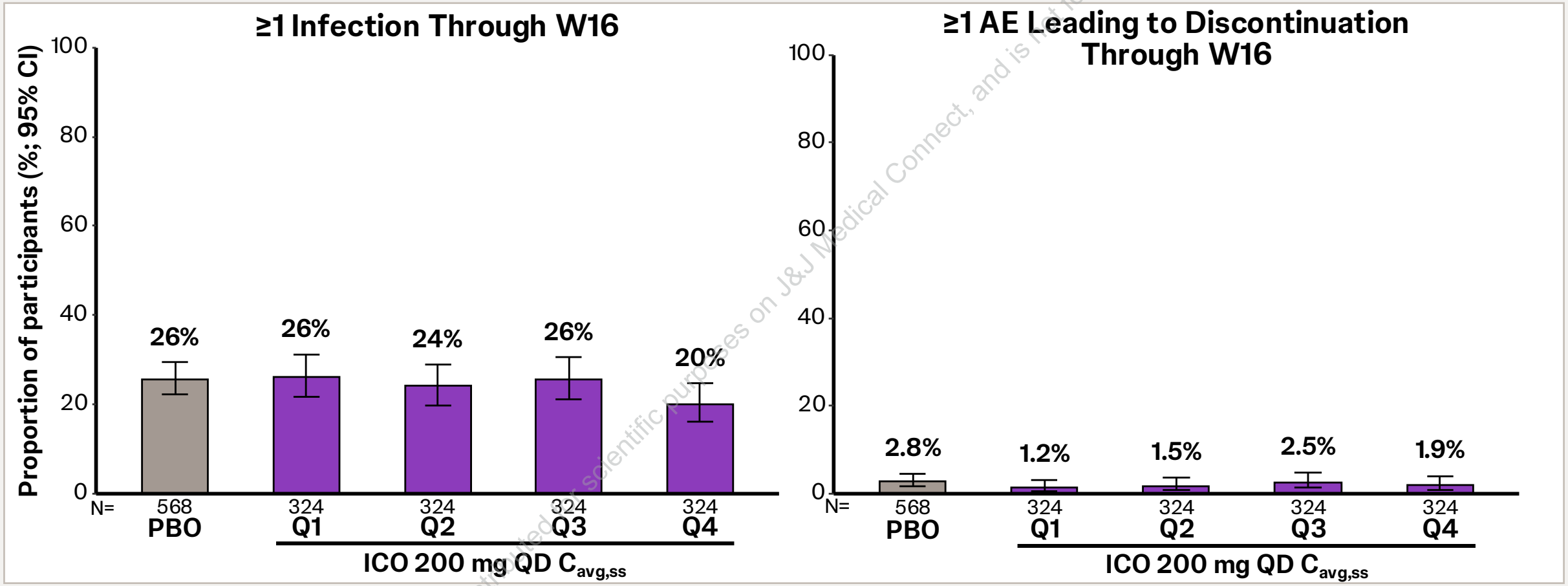
Includes data from ICONIC-TOTAL. $C_{avg,ss}$ quartile ranges: Q1: 441 to 0.966 ng/mL; Q2: 0.969 to 1.27 ng/mL; Q3: 1.29 to 1.78 ng/mL; Q4: 1.81 to 8.94 ng/mL.

AE incidence rates were similar across ICO 200 mg QD exposure quartiles and with placebo in 4 pooled RCTs



Includes data from ICONIC-LEAD, ICONIC-ADVANCE 1, ICONIC ADVANCE 2, and ICONIC TOTAL. $C_{avg,ss}$ quartile ranges: Q1: <0.96 ng/mL; Q2: ≥0.96 to <1.29 ng/mL; Q3: ≥1.29 to <1.86 ng/mL; and Q4: ≥1.86 ng/mL. **SAE**=serious adverse event.

AE incidence rates were similar across ICO 200 mg QD exposure quartiles and with placebo in 4 pooled RCTs



Includes data from ICONIC-LEAD, ICONIC-ADVANCE 1 & 2, and ICONIC TOTAL. $C_{avg,ss}$ quartile ranges: Q1: <0.96 ng/mL; Q2: ≥0.96 to <1.29 ng/mL; Q3: ≥1.29 to <1.86 ng/mL; Q4: ≥1.86 ng/mL.

Key Takeaways

- **ICO 200 mg QD demonstrated high rates of skin clearance and a favorable safety profile in adults and adolescents with moderate-to-severe PsO or at least moderate high-impact site PsO**
  - ✓ **ICO 200 mg QD provided consistently high W16 response rates across exposure quartiles compared with PBO**
  - ✓ **ICO 200 mg QD AE rates through W16 were consistent across exposure quartiles and similar to PBO**
- **Taken together, these findings support ICO 200 mg QD as an effective regimen for treating adults and adolescents with moderate-to-severe plaque PsO, including those with high-impact site involvement**

References

1. Armstrong AW. *JAMA*. 2020;323:1945-60.
2. Fourie AM. *Sci Rep*. 2024;14:17515.
3. Bissonnette R. *N Engl J Med*. 2025;393:1784-95.
4. Stein Gold L. *Lancet*. 2025;406:1363-74.
5. Gooderham M. *NEJM Evid*. 2025;4:EVIDoa2500155. doi: 10.1056/EVIDoa2500155

Acknowledgments

- The authors would like to thank Yingyi Li for pharmacometric support. Medical writing support was provided by JSS Medical Research under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med*. 2022;175:1298-1304).

- This presentation was sponsored by Johnson & Johnson.