Comparative analysis of icotrokinra and approved advanced treatments for achievement of completely clear skin in patients with moderate-to-severe psoriasis: A systematic literature review and network meta-analysis

AUTHORS: April Armstrong[1], Mahmoud Hashim[2], Lara Feghelm[3], Ya-Wen Yang[3], Tim Disher[4] AFFILIATIONS: [1]University of California, Los Angeles, USA; [2]Johnson & Johnson, Leiden, the Netherlands; [3]Johnson & Johnson, Horsham, PA, USA; [4]Sandpiper Analytics, Halifax, Canada

Summary

A comparative analysis of ICO and approved advanced treatments for PsO indicates:

- ICO was comparable to the IL-23 injectables in achieving completely clear skin
- ICO was superior to advanced oral therapies in achieving completely clear skin
  - The results were consistent for PASI 100 and IGA 0 NMA
- ICO may provide PsO patients with a treatment option that delivers high rates of completely clear skin via their preferred once-daily pill[4,5]
- Future NMA analyses will consider long-term data

Background

- Advances in therapy for moderate-to-severe psoriasis (PsO) treatment have made achieving completely clear skin a realistic treatment goal.[1]
- A recent survey in the US (web-based survey of 393 patients with PsO and 200 US healthcare professionals), confirmed that skin symptoms remain the main source of burden for most patients with PsO. Patients and providers expressed preference for oral PsO treatment over topical or injectable alternatives.[2,3]
- Icotrokinra (ICO), an investigational product at time of analyses, is a targeted oral peptide that selectively binds the interleukin-23 (IL-23) receptor and precisely inhibits IL-23 pathway signaling.
- ICO has been evaluated in participants with moderate-to-severe PsO in three Phase 3 studies (LEAD, ADVANCE1 and 2).[4,5]
- ICO demonstrated significantly higher rates of completely clear skin, as measured by rates of PASI 100 and IGA 0 response, compared to placebo and deucravacitinib.[4,5]
- Several factors are considered by healthcare providers and patients when evaluating treatment options, including comparative effectiveness and tolerability; the patient's overall disease burden, including signs, symptoms, and quality of life; and the preferred route of treatment administration.

Objectives

As head-to-head randomized clinical trial (RCT) data are currently limited in PsO, this network meta-analysis (NMA) aims to conduct a comparative analysis of ICO vs. approved advanced therapies for achievement of completely clear skin.

Methods

Systematic Literature Review

- A systematic literature review (SLR) was conducted in March 2025 following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles.[6]
  - RCTs in adults were included; treatment was restricted to biologics and advanced oral treatments at approved doses.
  - sPGA 0 or PGA 0 were considered similar to IGA 0, consistent with previous IGA NMAs.[7]

NMA Model Approach

- The analyses used a strict week 16 timepoint to ensure comparability.
- Random-effects Bayesian NMAs are presented to best account for potential between-trial heterogeneity.
- Model convergence was confirmed with no inconsistency detected.
- Baseline risk adjustment was deemed unnecessary due to near-zero placebo responses.

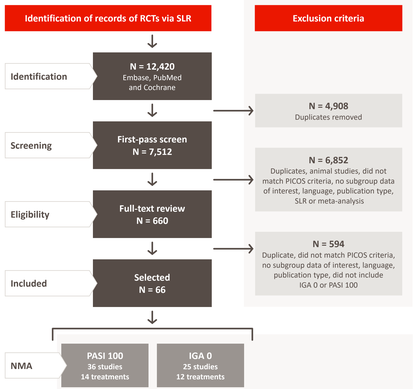
Result Interpretation Framework

- Chosen for consistency with previously published Bayesian analyses:[8]
  - "ICO is better": point estimate favors ICO and 95% CrI excludes null.
  - "ICO is favored": CrI crosses null but probability ≥85%.
  - "ICO is comparable": probability of 15%–85%.

Results

Among 12,420 identified records; 66 were eligible for inclusion in the quantitative NMA.

PRISMA diagram



NMA Comparators

Mechanism of action	Treatment included in NMA
-	• Placebo
IL-23p19 inhibitor	• Guselkumab (GUS) • Risankizumab (RIS)
IL-17 inhibitor	• Brodalumab (BRO) • Ixekizumab (IXE) • Secukinumab (SEC) • Bimekizumab (BIM)
TNF inhibitor	• Adalimumab (ADA) • Certolizumab (CER) 400/200 mg and 400/400 mg
IL-12/-23 inhibitor	• Ustekinumab (UST)
TYK-2 inhibitor	• Deucravacitinib (DEU)
PDE4 inhibitor	• Apremilast (APR)

IL, interleukin; PDE, phosphodiesterase; TNF, tumor necrosis factor; TYK, tyrosine kinase

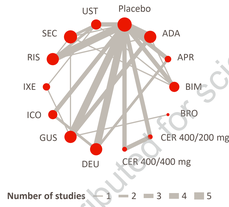
NMA model approach

- The random-effects models demonstrated adequate fit, with residual deviance closely approximating the number of data points. DIC values were comparable between fixed-effects and random-effects models across all analyses (ΔDIC <2), indicating no strong preference for either specification.
- Despite this, random-effects models were retained as a conservative approach, to account for potential clinical and methodological heterogeneity across trials.

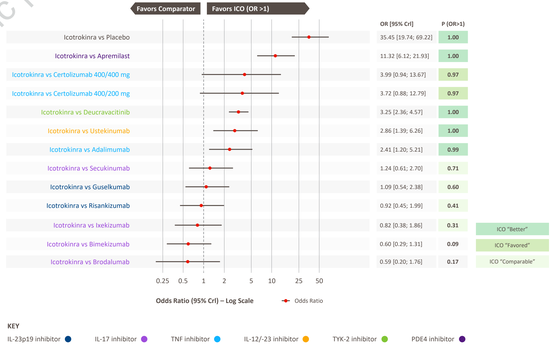
PASI 100 NMA: The probability of achieving completely clear skin at week 16 was found to be "better" with ICO than APR, DEU, UST, and ADA; "favored" over CER; and "comparable" with SEC, GUS, RIS, and IXE.

- BIM and BRO were found to be "favored" over ICO for achievement of PASI 100.

PASI 100 NMA: 36 RCTs and 14 Treatments



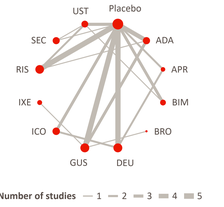
PASI 100 NMA: ICO vs. Comparators



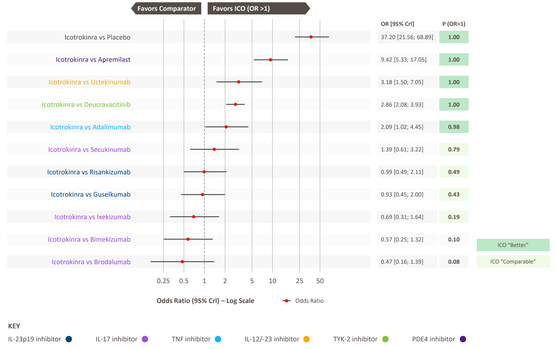
IGA 0 NMA: The probability of achieving completely clear skin at week 16 was found to be "better" with ICO than APR, UST, DEU, and ADA and "comparable" with SEC, RIS, GUS, and IXE, consistent with PASI 100 findings

- BIM and BRO were found to be "favored" over ICO for achievement of IGA 0.

IGA 0 NMA: 25 RCTs and 12 Treatments



IGA 0 NMA: ICO vs. Comparators



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CONTACT INFORMATION: Mahmoud Hashim, PhD | Email: Mhashi14@ITS.JNJ.com