Indirect comparison of the short-, mid-, and long-term efficacy of treatments for moderate to severe plaque psoriasis: a systematic review and network meta-analysis

April Armstrong,[1] Richard B. Warren,[2] Yichen Zhong,[3] Joe Zhuo,[3] Allie Cichewicz,[4] Ananth Kadambi,[4] Daniela R. Junqueira,[4] Tracy Westley,[4] Renata Kisa,[3] Carolin Daamen,[3] Matthias Augustin[5]

[1]University of Southern California, Los Angeles, CA; [2]The University of Manchester, Manchester, UK; [3]Bristol Myers Squibb, Princeton, NJ; [4]Evidera, Bethesda, MD; [5]University Medical Center, Hamburg, Germany

Synopsis

- Patients with moderate to severe plaque psoriasis have several systemic treatment choices available, including oral nonbiologic and biologic options
- Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, demonstrated superior efficacy versus apremilast and placebo in two phase 3 randomized controlled trials (RCTs) and is approved by the US Food and Drug Administration for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy
- This systematic literature review (SLR) and network meta-analysis (NMA) indirectly compared the efficacy of deucravacitinib with that of other approved, relevant systemic biologic and nonbiologic treatments over short-, medium-, and long-term follow-up; multinomial random effects models estimated improvement in responses on the Psoriasis Area and Severity Index (PASI) at Weeks 10–16, 24–28, and 44–60
- PASI 75 (75% improvement in PASI) response rate with deucravacitinib was comparable to that of first-generation biologics at Week 16, and higher at Week 24; at Week 52, it was comparable to that of the most effective first-generation biologics

Objective

- The objective of this analysis was to examine the clinical efficacy associated with deucravacitinib and other selected active biologic and nonbiologic treatments in patients with moderate to severe psoriasis

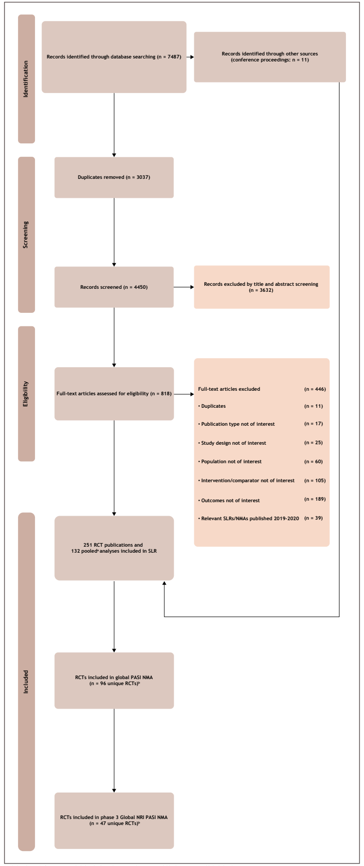
Methods

- Electronic databases were searched through October 2021 for RCTs of systemic treatments in adults with moderate to severe psoriasis who reported improvement in response on PASI
- Phase 3 trial data were included when:
  - Nonresponder imputation was applied[1,2]
  - Studies were conducted in multiple or single countries with diverse ethnic representation
- NMA was performed using multinomial random effects models adjusting for baseline risk (ie, placebo response) to estimate PASI responses over short-, mid-, and long-term follow-up periods (Weeks 10–16, 24–28, and 44–60, respectively) and reported following the PRISMA Reporting Guidelines for meta-analysis[3]

Results

- The SLR identified 47 phase 3 RCTs that applied nonresponder imputation and were included in the NMA (**Figure 1 and Figure 2A**); the mid-term analysis included 28 studies (**Figure 2B**); the long-term analysis included 21 studies (**Figure 2C**)

Figure 1. PRISMA flow diagram



Identification

Records identified through database searching (n = 7487)

Records identified through other sources (conference proceedings: n = 11)

Screening

Duplicates removed (n = 3037)

Records screened (n = 4450)

Records excluded by title and abstract screening (n = 3632)

Eligibility

Full-text articles assessed for eligibility (n = 818)

Full-text articles excluded	(n = 446)
• Duplicates	(n = 11)
• Publication type not of interest	(n = 17)
• Study design not of interest	(n = 25)
• Population not of interest	(n = 60)
• Intervention/comparator not of interest	(n = 105)
• Outcomes not of interest	(n = 189)
• Relevant SLRs/NMAs published 2019-2020	(n = 39)

Included

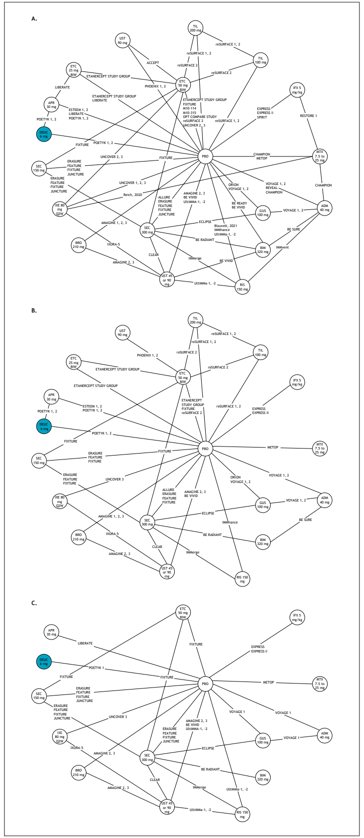
251 RCT publications and 132 pooled[a] analyses included in SLR

RCTs included in global PASI NMA (n = 96 unique RCTs)[b]

RCTs included in phase 3 Global NRI PASI NMA (n = 47 unique RCTs)[b]

[a]Pooled analyses of RCTs were not included in the SLR unless unique data were available that were not published elsewhere.
[b]RCTs eligible for Global PASI NMA and phase 3 global NRI PASI NMA, including POETYK PSO-1 and POETYK PSO-2.
NMA, network meta-analysis; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; RCT, randomized controlled trial; SLR, systematic literature review.

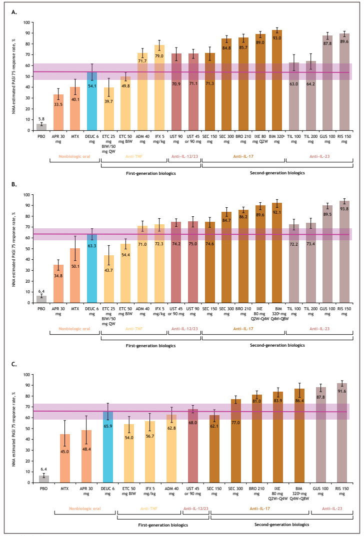
Figure 2. Network plots of trials included in the short-term (10–16 weeks; A), mid-term (24–28 weeks; B), and long-term (44–60 weeks; C) analyses



ACT, acitretin; ADM, adalimumab; APR, apremilast; BIM, bimekizumab; BIW, twice weekly; BRO, brodalumab; DEUC, deucravacitinib; ETC, etanercept; GUS, guselkumab; IFX, infliximab; IXE, ixekizumab; MTX, methotrexate; PBO, placebo; RIS, risankizumab; Q2W, once every 2 weeks; SEC, secukinumab; TIL, tildrakizumab; UST, ustekinumab.

- PASI 75 response rate with deucravacitinib at Week 16 (54.1%; credible interval [CrI], 46.5%, 61.6%) was within range of the first-generation biologics (range, 39.7 [CrI, 31.6%, 48.3%] for etanercept 25 mg to 79.0% [CrI, 74.0%, 83.5%] for infliximab; **Figure 3A**)
- PASI 75 response with deucravacitinib increased at Week 24 to 63.3% (CrI, 58.0%, 68.4%; **Figure 3B**)
- At Week 52, the PASI 75 response rate for deucravacitinib (65.9%; CrI, 58.0%, 73.4%) was comparable to that of the most effective first-generation biologics — adalimumab (62.8%; CrI, 55.3%, 69.6%) and ustekinumab (68.0%; CrI, 64.6%, 71.5%; **Figure 3C**)
- Newer IL-17 and IL-23 inhibitors showed the highest PASI 75 response rates of the included treatments, across all time points

Figure 3. Short-term estimated PASI 75 response,[a] posterior median and 95% CrI. Weeks 10–16 (A), mid-term estimated PASI 75 response for Weeks 24–28 (B), and long-term estimated PASI 75 response for Weeks 44–60 (C)



[a]Adjusted for placebo response rates.
[b]BIM is not approved for use in the United States.
Note: posterior median value given for each therapy; error bars represent 95% CrI.
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Conclusions

- Among oral nonbiologic treatments, deucravacitinib provided the best efficacy across time points compared with methotrexate and apremilast
- The PASI 75 response rates for deucravacitinib were within the range of those for first-generation biologics at Weeks 10–16 and 24–28
- At 1 year, the PASI 75 response rate for deucravacitinib was similar to that of adalimumab and ustekinumab
- The psoriasis treatment paradigm is changing with the approval of deucravacitinib, a convenient oral therapy with a long-term efficacy level similar to that of some biologic therapies

References

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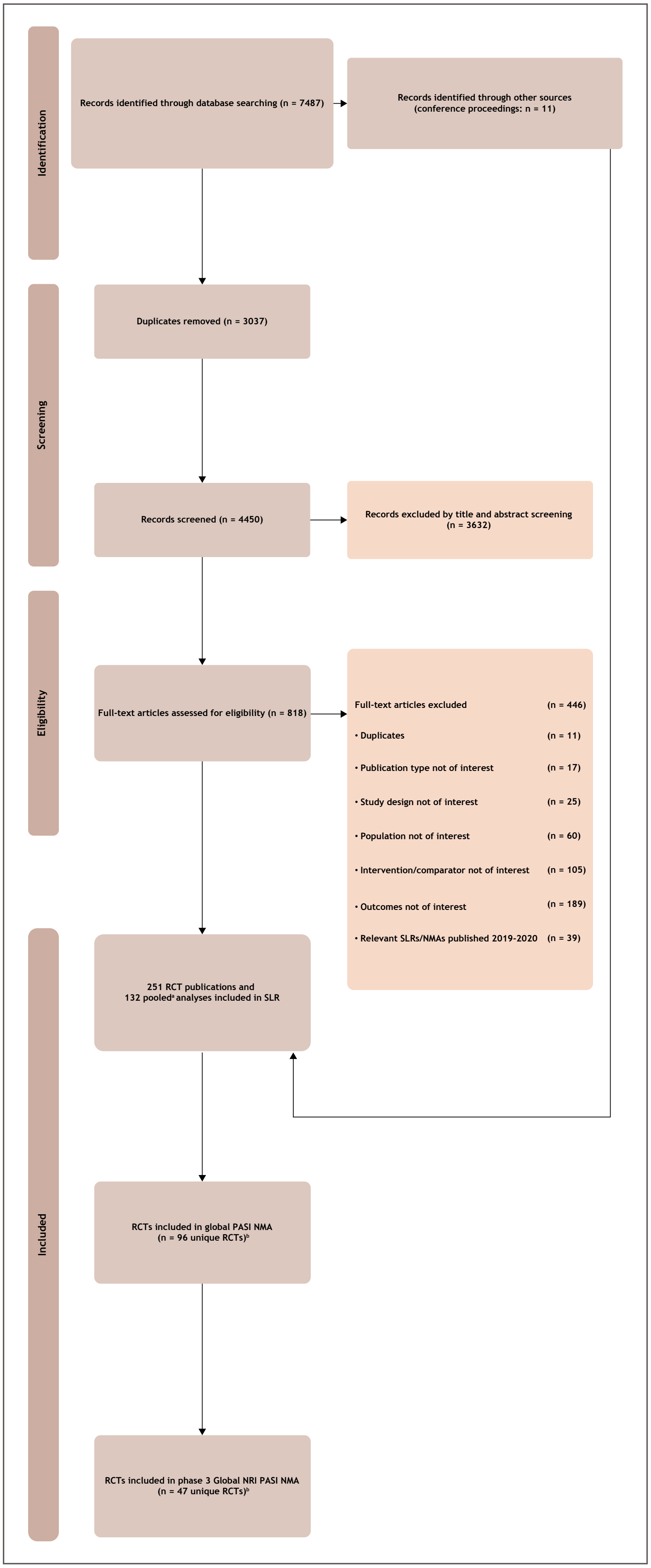

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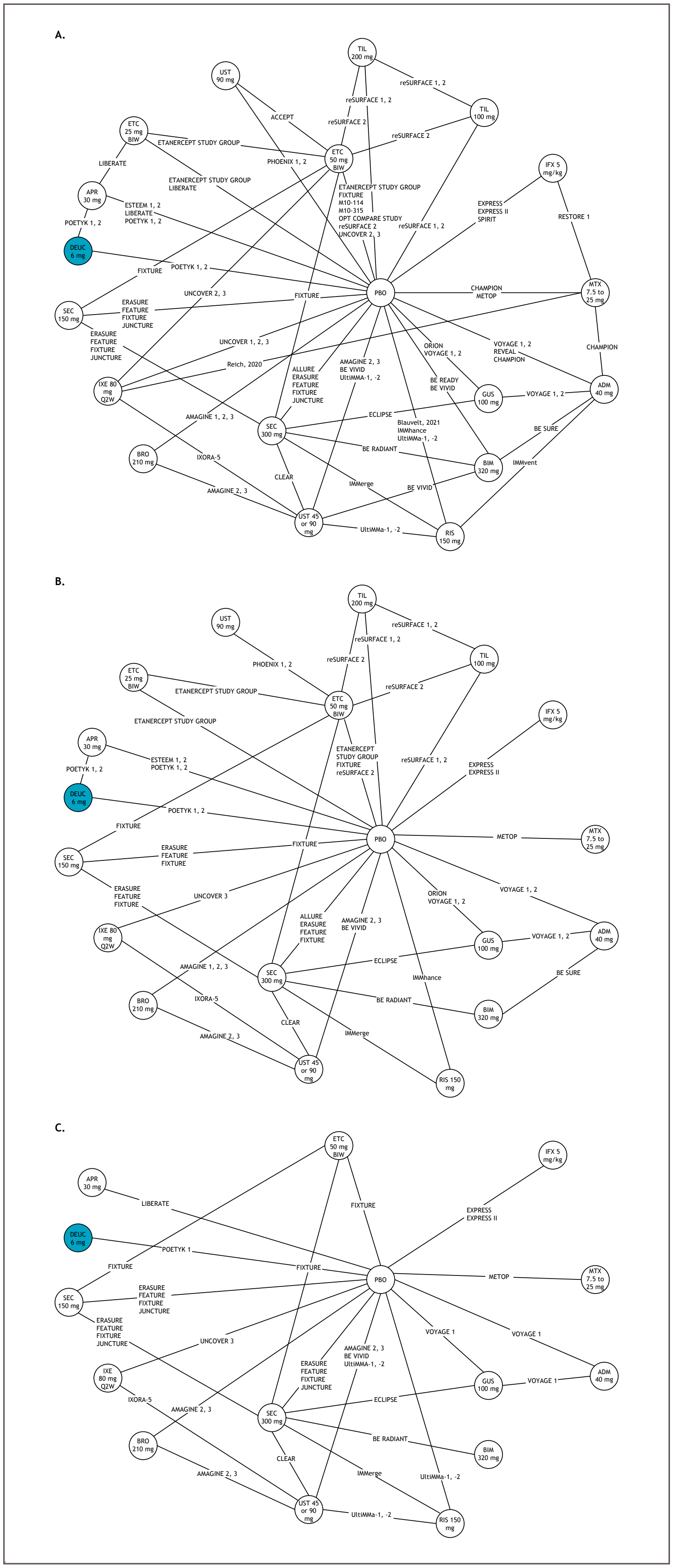

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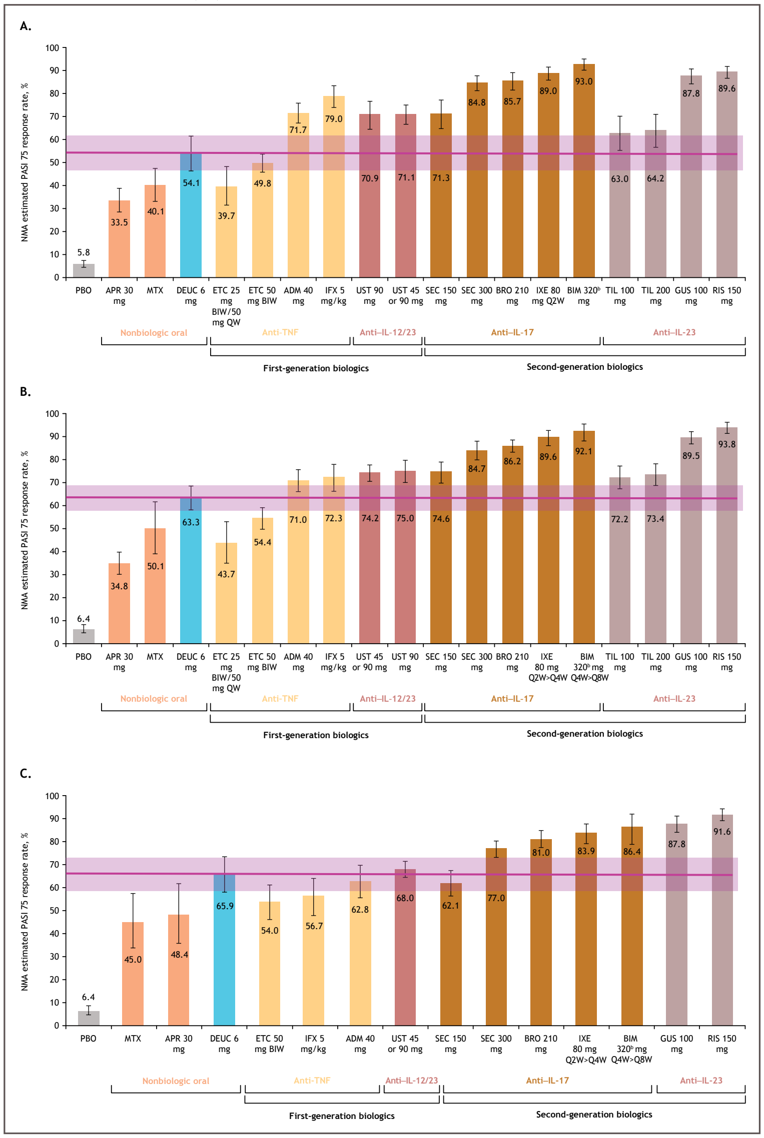

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