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]

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

Background

- 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

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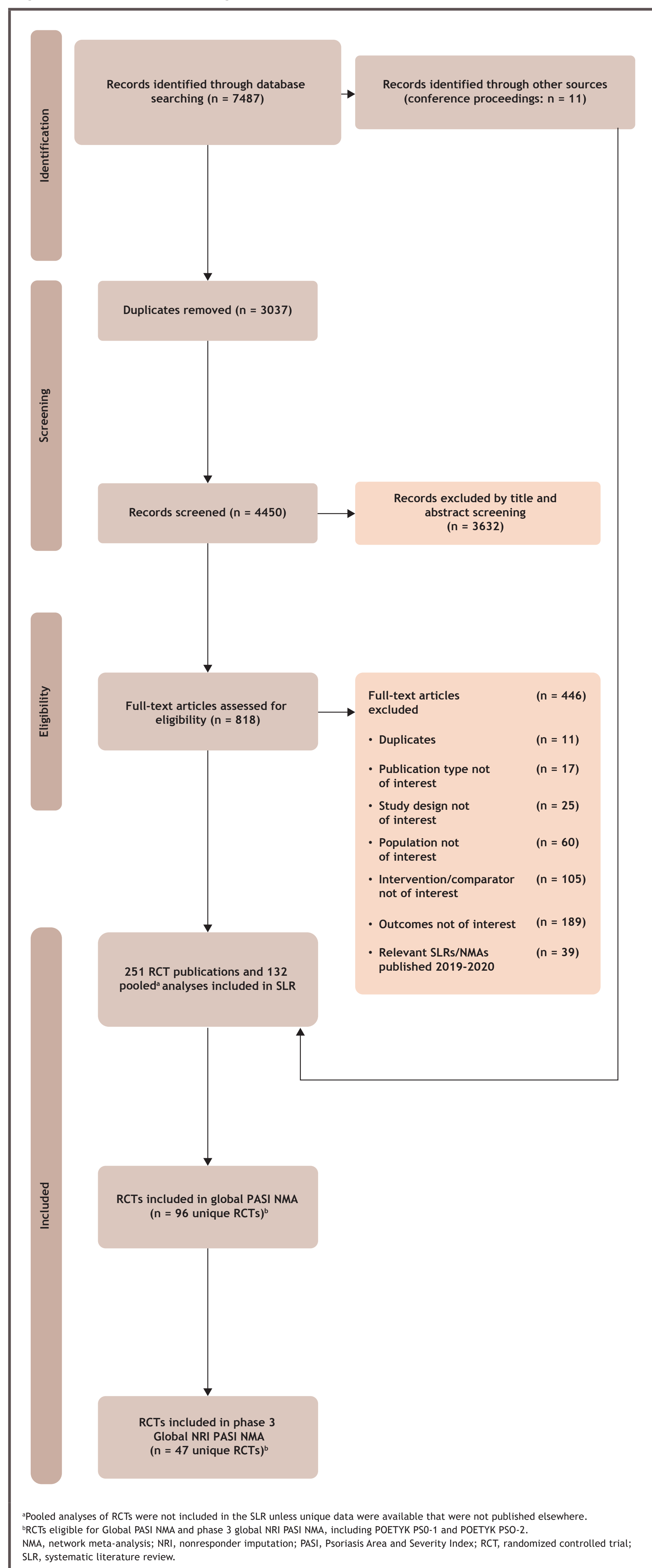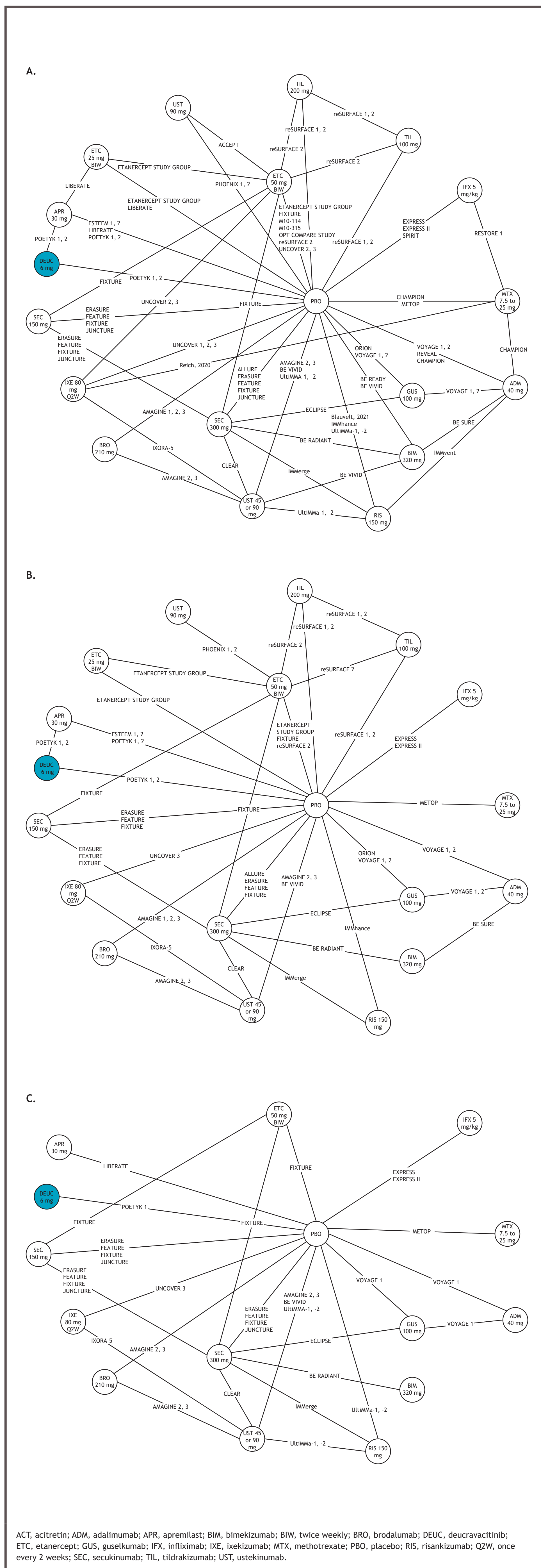
Figure 2. Network plots of trials included in the short-term (10–16 weeks; A), mid-term (24–28 weeks; B), and long-term (44–60 weeks; C) analyses

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.
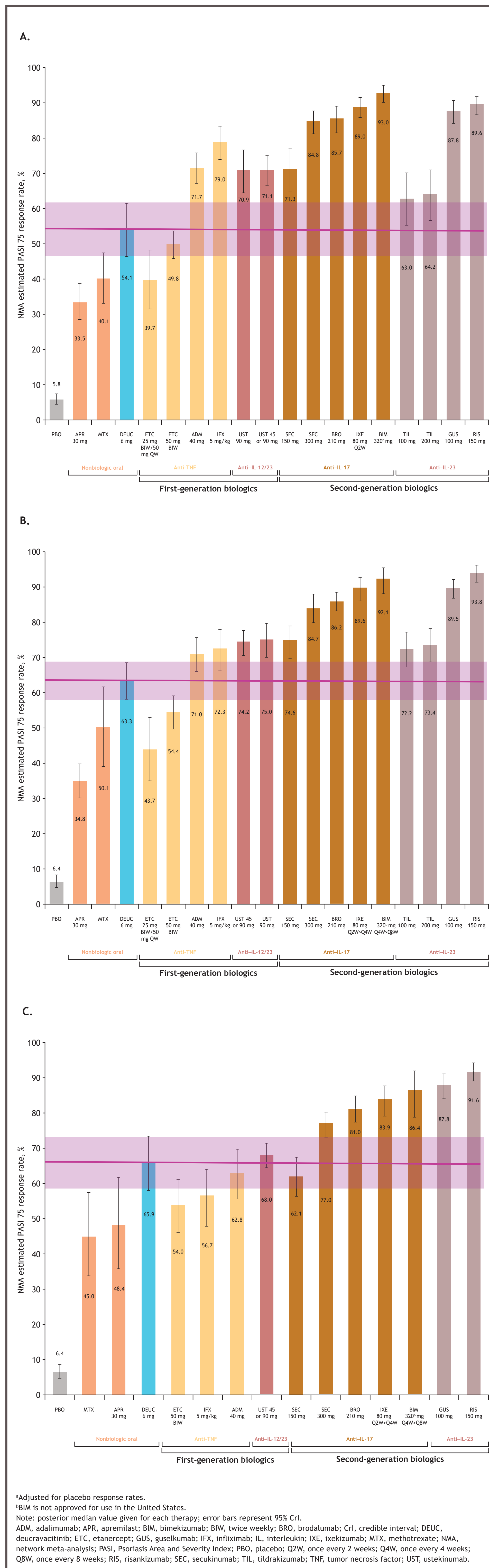
- PASI 75 response rate with deucravacitinib at Week 16 (54.1%; credible interval [Crl], 46.5%, 61.6%) was within range of the first-generation biologics (range, 39.7 [Crl, 31.6%, 48.3%] for etanercept 25 mg to 79.0% [Crl, 74.0%, 83.5%] for infliximab; Figure 3A)
- PASI 75 response with deucravacitinib increased at Week 24 to 63.3% (Crl, 58.0%, 68.4%; Figure 3B)
- At Week 52, the PASI 75 response rate for deucravacitinib (65.9%; Crl, 58.0%, 73.4%) was comparable to that of the most effective first-generation biologics — adalimumab (62.8%; Crl, 55.3%, 69.6%) and ustekinumab (68.0%; Crl, 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% Crl. 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% Crl.
ADM, adalimumab; APR, apremilast; BIM, bimekizumab; BIW, twice weekly; BRO, brodalumab; Crl, credible interval; DEUC, deucravacitinib; ETC, etanercept; GUS, guselkumab; IFX, infliximab; IL, interleukin; IXE, ixekizumab; MTX, methotrexate; NMA, network meta-analysis; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q2W, once every 2 weeks; Q4W, once every 4 weeks; Q8W, once every 8 weeks; RIS, risankizumab; SEC, secukinumab; TIL, tildrakizumab; TNF, tumor necrosis factor; UST, ustekinumab.

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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Email for April Armstrong, MD, MPH: AprilArmstrong@post.harvard.edu
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