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

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Synopsis

- The objective of this analysis was to examine the clinical efficacy of treatments for moderate to severe plaque psoriasis with oral nonbiologic and biologic options.
- This systematic literature review (SLR) and network meta-analysis (NMA) indirectly compared the efficacy of treatments with different routes of administration (oral vs. injection) and different pharmacological classes.

Objective

- The objective of this analysis was to examine the clinical efficacy of oral treatments for moderate to severe plaque psoriasis with nonbiologic and biologic options.

Methods

- Electronic databases were searched through October 2021 for RCTs of systemic treatments in adults with moderate to severe psoriasis who reported improvement in PASI at 12 weeks.
- Phase 3 trial data were included when:
  - Nonresponder imputation was applied.
  - 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 response rates with 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.

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).

Conclusions

- Among oral nonbiologic treatments, deucravacitinib provided the best efficacy across all time points compared with methotrexate and placebo.
- 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 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.

References

1. Guidance on Missing Data in Confirmatory Clinical Trials. European Medicines Agency; 2010. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/09/WC500176549.pdf
2. Guidance for Sponsors, Clinical Investigators, and IRBs. US Food and Drug Administration; 2008. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM070106.pdf
3. Page KJ, et al. PLoS Med. 2021;18:e1003583.

Acknowledgments

This study was sponsored by Bristol-Myers Squibb.

Disclosures

- AK: Grants and personal fees: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Biocryst Pharmaceuticals/Roche, Coliger, Dermotitis, Genentech, GlaxosmithKline, MedImmune, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Schering CT, Sun Pharma, and UCB; Consulting fees: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Schering CT, Sun Pharma, and UCB; Honoraria: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Schering CT, Sun Pharma, and UCB; Travel, accommodation, and expenses: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Schering CT, Sun Pharma, and UCB.
- RP: Research grants: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, MedImmune, Novartis, Pfizer, Regeneron, Schering CT, Sun Pharma, and UCB; Consulting fees: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Schering CT, Sun Pharma, and UCB; Honoraria: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Schering CT, Sun Pharma, and UCB; Travel, accommodation, and expenses: AbbVie, Biocryst Pharmaceuticals, Genentech, GlaxosmithKline, Novartis, Pfizer, Regeneron, Schering CT, Sun Pharma, and UCB.

Disclosure for all authors. To view a complete list, visit editorialia.com.

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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)
Objective

This systematic literature review (SLR) and network meta-analysis (NMA) compared short-, mid-, and long-term efficacy of treatments for moderate to severe plaque psoriasis. The aim was to indirectly compare several systemic treatment choices available, including oral nonbiologic (apremilast) and nonbiologic treatments in patients with moderate to severe plaque psoriasis.

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Figure 1. PRISMA flow diagram

Records identified through database searching (n = 7487)

Duplicates removed (n = 3037)

Records screened (n = 4450)

Outcomes not of interest (n = 189)

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

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

Full-text articles excluded (n = 446)

- Duplicates (n = 11)
- Publication type not of interest (n = 124)
- Study design not of interest (n = 46)
- Population not of interest (n = 160)
- Intervention/comparator not of interest (n = 105)
- Outcomes not of interest (n = 16)

251 RCT publications and 122 pooled analyses included in SLR

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

RCTs included in phase 3 Global MR PASI NMA (n = 47 unique RCTs)

*PASIs* are measures of skin disease severity and are quantified on a 0–72 scale. Higher PASI scores indicate worse disease severity.
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.
- 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, 55.5%, 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)
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

1. Guideline on Missing Data in Confirmatory Clinical Trials. European Medicines Agency; 2010. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-missing-data-confirmatory-clinical-trials_en.pdf
2. Guidance for Sponsors, Clinical Investigators, and IRBs. US Food and Drug Administration; 2008. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126489.pdf
3. Page MJ, et al. PLoS Med. 2021;18:e1003583.

Acknowledgments

- This study was sponsored by Bristol Myers Squibb.
- Medical writing and editorial assistance was provided by Cheryl Jones of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosures

- AA: Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Jansen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Celgene, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work
- RBW: Research grants: AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Jansen, Leo Pharma, Novartis, Pfizer, and UCB; Consulting fees: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, DICE, Eli Lilly, Jansen, Leo Pharma, Novartis, Pfizer, Sanofi, UCB, and UNION
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