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, 1 Yichan Zhong, 1 Joe Zuo, 1 Allie Ciechewicz, 1 Ananth Kadambi, 1 Daniela R. Junqueira, 1 Tracy Westley, 1 Renata Kisa, 1 Carolin Daamen, 1 Matthias Augustin 1

University of Southern California, Los Angeles, CA; The University of New Castle, Newcastle, UK; Eli Lilly and Company, Princeton, NJ; Kravis, Bethesda, MD; University Medical Center, Hamburg, Germany

Summary

• Patients with moderate to severe plaque psoriasis have several systemic treatments choices available, including oral nonbiologic and biologic options.

• First-generation biologics, such as TNF blockers, and second-generation biologics, such as IL-12/23, IL-23, and IL-17 biologics, have been effective in reducing skin lesions and improving patient-reported outcomes.

• TNF antagonists, such as etanercept, infliximab, and adalimumab, have been the most commonly used biologics in psoriasis treatment.

• TNF antagonists have demonstrated efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• TNF antagonists have been shown to provide long-term efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• Second-generation biologics, such as IL-12/23, IL-23, and IL-17 biologics, have also demonstrated efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• Second-generation biologics have been shown to provide long-term efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• The use of third-generation biologics, such as IL-22 biologics, has also been shown to provide efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• Third-generation biologics have been shown to provide long-term efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• The use of combination therapies, such as biologic and nonbiologic agents, has also been shown to provide efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

• Combination therapies have been shown to provide long-term efficacy in reducing skin lesions and improving patient-reported outcomes in patients with moderate to severe plaque psoriasis.

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 plaque 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 to PASI.

• Phase 3 trial data were included when:
  • No nonresponder imputation was applied.
  • Studies were conducted in multiple or single countries with diverse ethnic representation.

• NMA was performed using uninformative random effects models adjusting for baseline risk (ie, placebo response) to estimate NRS 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-analyses.

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).

• PASI 75 response rate with deucravacitinib at Week 16 (54.1%; credible interval [CI], 46.5%, 61.6%) was within range of the first-generation biologics’ range, 39.7% (CI, 31.6%, 48.3%) for etanercept 25 mg vs 79.0% (CI, 74.0%, 83.5%) for infliximab.

• PASI 75 response with deucravacitinib increased at Week 24 to 63.3% (CI, 58.0%, 68.6%; Figure 2B) and at Week 52, the PASI 75 response rate for deucravacitinib (68.9%; CI, 63.0%, 74.4%) was comparable to that of the most effective first-generation biologics – adalimumab (62.8%; CI, 55.3%, 69.6%) and ustekinumab (62.0%; CI, 54.1%, 70.3%; Figure 2C)

• Lower IL-17 and IL-23 inhibitors showed the highest PASI 75 response rates of the included treatments across all time points.

• Figure 3A shows the short-term estimated PASI 75 response, posterior median and 95% CI at 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


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• AK grants and personal fees: AbbVie, Eli Lilly, Amgen, Boehringer Ingelheim, Pfizer, Regeneron, Sanofi Genzyme, Science III, Sanofi, and Viatrazagro. Grants and personal fees: Janssen, Leo Pharma, Novartis, Pfizer, and UCB; Consulting fees: AbbVie, Eli Lilly, Janssen, and Viatrazagro; Advisory boards: Amgen, Boehringer Ingelheim, Janssen, and Science III; Employment: Evidera, a company that provides consulting and other research services to Bristol Myers Squibb.

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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, Richard B. Warren, Yi Chen Zhong, Joe Zhuo, Allie Cichewicz, Ananth Kadambi, Daniela R. Junqueira, Tracy Westley, Renata Kisa, Carolin Daamen, Matthias Augustin

Abstract

Objective

Patients with moderate to severe plaque psoriasis have tried several therapies to control their disease. This review aimed to compare the short-, mid-, and long-term efficacy of treatments for moderate to severe plaque psoriasis, with a focus on active biologics and nonbiologics in patients with diverse ethnic representation.

Methods

A systematic review with network meta-analysis (NMA) was conducted to compare the short-, mid-, and long-term estimated PASI 75 response for active biologics and nonbiologics. The literature search included electronic databases through October 2021, and results were presented at the Fall Clinical Dermatology Conference in October 2020.

Results

The short-term analysis included 3632 studies and 21 unique RCTs for the most effective first-generation biologics (range, 39.7 [CrI, 31.6%, 48.3%] for IXORA-5). The mid-term analysis included 3632 studies and 21 unique RCTs for first-generation biologics (range, 58.0% [CrI, 48.3%, 68.4%] for FIXTURE). The long-term analysis included 21 studies and 21 unique RCTs for the most effective first-generation biologics (range, 65.9% [CrI, 58.0%, 68.4%] for UNCOVER 1, 2, 3).

Conclusions

The psoriasis treatment paradigm is changing with the increased availability of more efficacious treatments. This review provides a comprehensive comparison of treatments for moderate to severe plaque psoriasis, offering insights into the efficacy of various therapies over different time periods.

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University of Southern California, Los Angeles, CA; The University of Manchester, Manchester, UK; Bristol Myers Squibb, Princeton, NJ; Evidera, Bethesda, MD; 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 at Week 16 (54.1%; Crl, 58.0%, 68.4%; Figure 3C) was comparable to that of the most effective 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)
Presented at the Fall Clinical Dermatology Conference; October 20

Methods

- PASI 75 (75% improvement in PASI) response rate with review and network meta-analysis

Indirect comparison of the short-, mid-, and long-term efficacy of treatments for moderate to severe plaque psoriasis: a systematic meta-analysis (NMA) indirectly compared the efficacy of therapy or phototherapy to severe plaque psoriasis who are candidates for systemic trials (RCTs) and is approved by the US Food and Drug Administration.

- NMA estimated PASI 75 response rate, %

<table>
<thead>
<tr>
<th>Therapy or Phototherapy</th>
<th>Week 16</th>
<th>Week 24</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective first-generation biologics</td>
<td>73.3</td>
<td>60.7</td>
<td>58.4</td>
</tr>
<tr>
<td>Similar to that of adalimumab and ustekinumab</td>
<td>63.4</td>
<td>56.7</td>
<td>56.0</td>
</tr>
<tr>
<td>Nonresponder imputation was applied with a long-term efficacy level similar to that of some biologic therapies within the range of those for first-generation biologics at 12/23.</td>
<td>71.3</td>
<td>68.0</td>
<td>65.5</td>
</tr>
</tbody>
</table>

### Reporting Guidelines for meta-analysis

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, 55.3%, 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,\textsuperscript{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


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Disclosures

- **AA**: Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, 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.
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Phase 3 trial data were included when:

**Objective**

- PASI 75 (75% improvement in PASI) response rate with

This systematic literature review (SLR) and network meta-analysis (NMA) indirectly compared the efficacy of treatments for moderate to severe plaque psoriasis: a systematic review and long-term follow-up; multinomial random effects models adjusting for baseline risk (ie, placebo response)

**Synopsis**

- Patients with moderate to severe plaque psoriasis have several systemic treatment choices available, including oral therapy or phototherapy

Studies were conducted in multiple or single countries with

Nonresponder imputation was applied 1,2

Figure 2C

Figure 2B

132 pooled analyses included in SLR (n = 96 unique RCTs)b

- Study design not of interest (n = 25)

**B.**

150 mg

30 mg

APR

100 mg

–

320b mg

50 mg

–

reSURFACE 1, 2

reSURFACE 2

M10-315

reSURFACE 2

SPIRIT RESTORE 1

SPIRIT FIXTURE

ESTEEM 1, 2

AMAGINE 1, 2, 3

ULTI

IMMerge

EXPERSS II

GUS

50 mg

30 mg

SEC

70

90

10

40

30

100 mg

40 mg

GUS

100 mg

IFX 5

100 mg

84.8 85.7

71.1

71.3

62.1

86.2 89.6 92.1 89.5

84.8 85.7

79.0 83.9 86.4

71.1

71.3

62.1

86.2 89.6 92.1 89.5

84.8 85.7

79.0 83.9 86.4

- First-generation biologics
- Second-generation biologics

**Grants and personal fees**

- AbbVie, Amgen, Boehringer Ingelheim, Celgene, Janssen Biotech, Leo Pharma, Merck, Novartis, Sun Pharma, and UCB; Investigator:
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