Optimizing the treatment sequence: the cumulative clinical benefit of treatment initiation with deucravacitinib versus apremilast over 52 weeks in patients with moderate to severe plaque psoriasis from the POETYK PSO-1 trial

April W. Armstrong, 1 Sang Hee Park, 2 Viktor Chirikov, 1 Pierre Nicolas, 1, 3 Wei-Jhih Wang, 4 Matthew J. Colombo, 1 Vardhanam Patel 1

1Department of Medicine, University of Southern California, Los Angeles, CA; 2Bristol Myers Squibb, Princeton, NJ; 3OPEN Health, Bethesda, MD; 4Bristol Myers Squibb, Boussy, Switzerland

Synopsis

• Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 inhibitor 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.

• In the recent phase 3 clinical trial POETYK PS-1, patients with moderate to severe plaque psoriasis were randomized 2:1 to deucravacitinib, placebo, or apremilast.

• Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index score (PASI 50) at Week 24 crossed over to deucravacitinib.

• At Week 52, 44.3% of these patients achieved at least 75% improvement from baseline in PASI score (PASI 75), and 42.6% achieved a static Physician Global Assessment score of 0 or 1.

• Patients receiving apremilast who achieved PASI 50 at Week 24 continued with apremilast.

• Patients who received placebo are not represented in this analysis.

• This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the treatment pathway that provides greater benefit to the patient.

• The cumulative clinical benefit reflects the total time patients spend in a state of therapeutic response.

• The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast.

Objective

• To evaluate the cumulative clinical benefit of initiating with deucravacitinib vs apremilast from baseline to Week 52 based on data from POETYK PSO-1.

Methods

• POETYK PSO-1 was a multicenter, randomized, double-blind, placebo- and active comparator–controlled study.

• Patients were aged ≥ 18 years and had moderate to severe plaque psoriasis (PASI score ≥ 10, sPGA score ≥ 3, and body surface area involvement ≥ 10%).

• Co-morbid efficacy endpoints were PASI 75 and PASI 90, and body surface area involved (BSA).

• Non-responder imputation was used for missing data.

• This post hoc analysis compared data from 2 arms in the POETYK PSO-1 trial (Figure 1).

• Deucravacitinib arm: patients initiated with and continued on deucravacitinib, regardless of response status after randomization.

• Apremilast initiators arm: patients initiated with apremilast at randomization, regardless of response status.

• Deucravacitinib initiators who continued deucravacitinib received placebo at Week 12 unless the patient did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index (PASI) score at Week 24.

Target population

Eligible patients were adults aged ≥ 18 years with moderate to severe plaque psoriasis (PASI score ≥ 10, sPGA score ≥ 3, and body surface area involvement ≥ 10%).

• Patients were randomized 2:1 to deucravacitinib or apremilast.

• Deucravacitinib initiators continued deucravacitinib at Week 12 unless the patient did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index (PASI) score at Week 24.

• Apremilast initiators continued apremilast at Week 12 unless the patient achieved at least 50% improvement from baseline in Psoriasis Area and Severity Index (PASI) score at Week 24.

• Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index score (PASI 50) at Week 24 crossed over to deucravacitinib.

• At Week 52, 44.3% of these patients achieved at least 75% improvement from baseline in PASI score (PASI 75), and 42.6% achieved a static Physician Global Assessment score of 0 or 1.

• Patients receiving apremilast who achieved PASI 50 at Week 24 continued with apremilast.

• Patients who received placebo are not represented in this analysis.

• This study determined the AUC using data at a patient level (responder status at each time point over 52 weeks).

• Cumulative clinical benefit from randomization to Week 52 was determined by the total area under the curve of each treatment arm, with the following stratification parameters:

| Parameter                        | Description                                                                 |
|----------------------------------|-----------------------------------------------------------------------------|
| Region                           | United States, China, Japan, rest of the world (ROW)                        |
| Body weight                      | <90 kg, ≥ 90 kg                                                             |
| Prior use of a biologic treatment| yes/no                                                                      |
| Age                              | ≥ 18 years                                                                   |
| Diagnosis                        | Moderate to severe plaque psoriasis                                          |
| Prior treatment                  | Systemic therapy or phototherapy                                            |

• The benefit ratio of initiating with deucravacitinib vs apremilast was 1.50.

• Figure 2 displays the standardized adjusted cumulative AUC for PASI 52 over 52 weeks.

• Deucravacitinib initiators spent ≈150% more time in therapeutic response over 1 year compared with apremilast initiators.

• Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive.

Results

PASI 75

• Standardized average cumulative PASI 75 response over 52 weeks among patients initiating with deucravacitinib was 57.3% compared with 38.2% in patients initiating with apremilast (117 patients who continued apremilast after failure to respond with apremilast at Week 24 and 54 patients who switched to deucravacitinib).

• The adjusted difference in AUC0–52wk was 955.69 (95% CI, 642.22–1269.16); P < 0.001.

• The benefit ratio of initiating with deucravacitinib vs apremilast was 1.58.

• Table 2 displays the standardized adjusted cumulative AUC for PASI 52 over 52 weeks.

Conclusions

• Initiating with deucravacitinib resulted in greater cumulative benefits over 52 weeks than initiating with apremilast.

• Deucravacitinib initiators spend ≈150% more time in therapeutic response over 1 year compared with apremilast initiators.

• Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive.

References

1. Armstrong AW, et al. J Am Acad Dermatol. 2022;96(1):e1-e16. [Epub ahead of print].

2. Armstrong AW, et al. [Poster] Presented at the American Academy of Dermatology Annual Meeting, March 25–29, 2022, Boston, MA.

3. Armstrong AW, et al. J Dermatolog Treat. 2017;28:200-205.

4. Budhathoki A, et al. Qual Life Res. 2011;20:181-191.

5. Warner RB, et al. Eur J Dermatol. 2020;30:452-467.

6. Brouwer A, et al. J Am Acad Dermatol. 2007;56:27-44.

Acknowledgments

• This study was supported by Bristol Myers Squibb.

• Medical writing and editorial assistance was provided by Eleanor Bush, Inc., of House Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Disclosures

• AWA: Grants and personal fees: Janssen, Bristol Myers Squibb, El Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Celgene, Dermotest, Genentech, GlaxoSmithKline, Helsa Therapeutics, Merck, Modernizing Medicine, Ortho-Dermatologics, Pfizer, Regeneron, Science 37, Sun Pharma, and Valeant; Grants: Grants: Dentsra, Kyna Hakko Kirin, and LCS, outside the submitted work.

• BHF, PNL: Employees of and may own stock options in Bristol Myers Squibb.

• WJN: Employees of OPEN Health, which has received consulting fees from Bristol-Myers Squibb.
Optimizing the treatment sequence: the cumulative clinical benefit of treatment initiation with deucravacitinib versus apremilast over 52 weeks in patients with moderate to severe plaque psoriasis from the POETYK PSO-1 trial

April W. Armstrong,1 Sang Hee Park,1 Viktor Chirikov,1 Pierre Nicolas,1,2 Wei-Jhii Wang,1 Matthew J. Colombo,1 Vardhaman Patel1

1Yale School of Medicine, University of Southern California, Los Angeles, CA; 2Bristol Myers Squibb, Princeton, NJ; 3OPEN Health, Bethesda, MD; 4Bristol Myers Squibb, Boudry, Switzerland

Abstract

This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the overall magnitude of clinical improvement over 52 weeks. The benefit ratio of initiating with deucravacitinib vs apremilast was 1.58 (p < 0.001). Deucravacitinib initiators spend ≈150% more time in therapeutic response over 1 year compared with apremilast initiators. This may optimize the clinical benefit that patients receive after failure to respond with apremilast.

Introduction

In the recent phase 3 clinical trial POETYK PSO-1, patients with moderate to severe plaque psoriasis were randomized 2:1:1 to deucravacitinib, placebo, or apremilast1 systemic therapy or phototherapy. This study determined the AUC using data at a patient level (responder status at each time point over time).

Methods

Prior use of a biologic treatment (yes/no), Region (United States, China, Japan, rest of the world [ROW]), Total body surface area involvement (%), and PASI 50 nonresponders were used as covariates. Using the baseline visit data, the AUC0–52wk was calculated, representing the relative cumulative clinical benefit of the 2 treatment initiators compared with the apremilast initiators. Ratios of AUC0–52wk were calculated, representing the relative cumulative clinical benefit of the 2 treatment initiators compared with the apremilast initiators.

Results

Deucravacitinib arm:

- Prior use of a biologic treatment (yes/no)
- Region (United States, China, Japan, rest of the world [ROW])
- Total body surface area involvement (%)
- PASI 50 nonresponders

Adjusted AUC0–52wk comparisons between the 2 treatment arms were based on an analysis of covariance (ANCOVA). This study determined the AUC using data at a patient level (responder status at each time point over time).

Outcomes

Coprimary efficacy endpoints were PASI 75 and sPGA 0/1. Nonresponder imputation was used for missing data. Ratios of AUC0–52wk were calculated, representing the relative cumulative clinical benefit of the 2 treatment initiators compared with the apremilast initiators.

The benefit ratio of initiating with deucravacitinib vs apremilast was 1.58 (p < 0.001). The adjusted difference in AUC0–52wk was 990.66 (95% CI, 683.37–1297.95); Adjusted AUC0–52wk [% × weeks] was 2612.82 in the deucravacitinib arm and 1657.13 in the apremilast arm.

Deucravacitinib initiators spend ≈150% more time in therapeutic response over 1 year compared with apremilast initiators. This may optimize the clinical benefit that patients receive after failure to respond with apremilast.

Conclusion

Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive.
Synopsis

- Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 inhibitor 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
- In the recent phase 3 clinical trial POETYK PSO-1, patients with moderate to severe plaque psoriasis were randomized 2:1:1 to deucravacitinib, placebo, or apremilast
  - Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index score (PASI 50) at Week 24 crossed over to deucravacitinib
    - At Week 52, 46.3% of these patients achieved at least 75% improvement from baseline in PASI score (PASI 75), and 42.6% achieved a static Physician Global Assessment (sPGA) score of 0 or 1 (sPGA 0/1)
  - Patients receiving apremilast who achieved PASI 50 at Week 24 continued with apremilast
  - Patients who received placebo are not represented in this analysis
- This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the treatment pathway that provides greater benefit to the patient
  - The cumulative clinical benefit reflects the total time patients spend in a state of therapeutic response
- The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast

Objective

- To evaluate the cumulative clinical benefit of initiating with deucravacitinib vs apremilast from baseline to Week 52 based on data from POETYK PSO-1

Methods

- POETYK PSO-1 was a multicenter, randomized, double-blind, placebo- and active comparator-controlled study
  - Patients were aged ≥18 years and had moderate to severe plaque psoriasis (PASI score ≥12, sPGA score ≥3, and body surface area involvement ≥10%)
  - Coprimary efficacy endpoints were PASI 75 and sPGA 0/1
  - Nonresponder imputation was used for missing data
- This post hoc analysis compared data from 2 arms in the POETYK PSO-1 trial (Figure 1)
  - Deucravacitinib arm: patients initiated with and continued on deucravacitinib, regardless of response status
  - Apremilast initiators arm: patients initiated with apremilast; at Week 24, PASI 50 responders continued with apremilast while PASI 50 nonresponders crossed over to deucravacitinib
- Cumulative clinical benefit from randomization to Week 52 was determined by the total area under the curve of clinical response over 52 weeks ($AUC_{0-52\text{wk}}$) in each arm
  - AUC analysis has been employed to evaluate outcomes over time in clinical trials, as the AUC reflects the rapidity and durability, as well as the magnitude, of response
  - While assessments at discrete time points identify static responses, the AUC approach captures cumulative treatment effects over time
  - This study determined the AUC using data at a patient level (responder status at each time point over 52 weeks)
- Total $AUC_{0-52\text{wk}}$ was calculated separately for each efficacy endpoint, using the trapezoidal rule
  - Total $AUC_{0-52\text{wk}} = \sum_{i=0}^{15} \frac{1}{2} (P_{i+1} + P_i) (T_{i+1} - T_i)$, where $T_i$ ($i = 0, 1, 2, 3, ..., 15$) denotes the time points of Weeks 0, 1, 2, 4, 8, 12, and 16, then every 4 weeks thereafter through Week 52, and $P_i$ denotes the response (yes = 1; no = 0) at each time point, $T_i$
- The result was standardized as a percentage of maximum possible $AUC_{0-52\text{wk}}$ (0-5200 [% × weeks]) and aggregated to the population level
- Adjusted AUC comparisons between the 2 treatment arms were based on an analysis of covariance (ANCOVA) model, with the following stratification parameters:
  - Prior use of a biologic treatment (yes/no)
  - Region (United States, China, Japan, rest of the world [ROW])
  - Body weight (<90 kg, ≥90 kg), in the United States and ROW only
- Ratios of $AUC_{0-52\text{wk}}$ were calculated, representing the relative cumulative clinical benefit of the 2 treatment pathways for achieving PASI 75 or sPGA 0/1 over the 52-week period

| Weeks | $AUC_{0-52\text{wk}}$ | Difference in estimate (95% CI) |
|-------|----------------------|--------------------------------|
| 30    | 2612.82              | -550.17 (-923.52 to -176.82)   |
| 60    | 5168.32              | -1265.60 (-2541.26 to -98.95)   |

Figure 1. Study design comparing data from 2 arms of POETYK PSO-1

Table 1. Cumulative clinical benefit measured by PASI 75 response over 52 weeks

| Treatment | Patients Initiating | PASI 75 at Week 24 | PASI 75 at Week 52 |
|-----------|---------------------|--------------------|--------------------|
| Deucravacitinib | 332                 | 87                 | 46.3% |
| Apremilast Initiators | 168               | 54                 | 31.9% |

Table 2. Cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks

| Treatment | Patients Initiating | sPGA 0/1 at Week 24 | sPGA 0/1 at Week 52 |
|-----------|---------------------|---------------------|---------------------|
| Deucravacitinib | 332                 | 50.2%               | 38.2%               |
| Apremilast Initiators | 168               | 31.9%               | 26.7%               |
Results

PASI 75
- Standardized average cumulative PASI 75 response over 52 weeks among patients initiating with deucravacitinib was 57.3% compared with 38.2% in patients initiating with apremilast (including 87 patients who continued apremilast after Week 24 and 54 patients who switched to deucravacitinib) (Table 1)
  - Adjusted AUC$_{0–52wk}$ [% × weeks] was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm
  - The adjusted difference in AUC$_{0–52wk}$ was 990.66 (95% CI, 683.37–1297.95); P < 0.001
  - The benefit ratio of initiating with deucravacitinib vs apremilast was 1.50
- Figure 2 displays the standardized adjusted cumulative AUC for PASI 75 over 52 weeks

sPGA 0/1
- Standardized average cumulative sPGA 0/1 response over 52 weeks among patients initiating with deucravacitinib was 50.2% compared with 31.9% in patients initiating with apremilast (Table 2)
  - Adjusted AUC$_{0–52wk}$ [% × weeks] was 2612.82 in the deucravacitinib arm and 1657.13 in the apremilast initiators arm
  - The adjusted difference in AUC$_{0–52wk}$ was 955.69 (95% CI, 642.22–1269.16); P < 0.001
  - The benefit ratio of initiating with deucravacitinib vs apremilast was 1.58
- Figure 3 displays the standardized adjusted cumulative AUC for sPGA 0/1 over 52 weeks

Table 1. Cumulative clinical benefit measured by PASI 75 response over 52 weeks

| Outcomes                   | Deucravacitinib, n = 332 | Apremilast Initiators, n = 168 | Difference in estimate (95% CI) | P value | Benefit ratio |
|----------------------------|---------------------------|--------------------------------|---------------------------------|---------|---------------|
| Adjusted AUC$_{0–52wk}$ [% × weeks] | 2978.72 (683.37–1297.95)   | 1988.06 (642.22–1269.16)        | 990.66 (95% CI)                | < 0.001 | 1.50          |

**Table 1.** Cumulative clinical benefit measured by PASI 75 response over 52 weeks

- Adjusted AUC$_{0–52wk}$ [% × weeks] was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm
- The adjusted difference in AUC$_{0–52wk}$ was 990.66 (95% CI, 683.37–1297.95); P < 0.001
- The benefit ratio of initiating with deucravacitinib vs apremilast was 1.50

Figure 2. Standardized adjusted AUC$_{0–52wk}$: PASI 75

- Adjusted AUC$_{0–52wk}$ [% × weeks] was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm
- The adjusted difference in AUC$_{0–52wk}$ was 990.66 (95% CI, 683.37–1297.95); P < 0.001
- The benefit ratio of initiating with deucravacitinib vs apremilast was 1.50
Table 2. Cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks

| Outcomes                              | Deucravacitinib, n = 332 | Apremilast Initiators, n = 168 | Difference in estimate (95% CI) | P value | Benefit ratio |
|----------------------------------------|--------------------------|-------------------------------|---------------------------------|---------|---------------|
| Adjusted AUC0–52wk, % × weeks          | 2612.82                  | 1657.13                       | 955.69 (642.22–1269.16)         | < 0.001 | 1.58          |
| Standardized average cumulative responseb | 50.2%                    | 31.9%                         | –                               | –       | –             |

aAmong patients initiating with apremilast, 87 achieved PASI 50 at Week 24 and continued receiving apremilast, and 54 did not achieve PASI 50 and switched to deucravacitinib.
bAUC0–52wk/maximum AUC0–52wk.

Figure 3. Standardized adjusted AUC0–52wk: sPGA 0/1

Conclusions

- Initiating with deucravacitinib resulted in greater cumulative benefits over 52 weeks than initiating with apremilast
  - Deucravacitinib initiators spend ≈150% more time in therapeutic response over 1 year compared with apremilast initiators
- Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive

References

1. Armstrong AW, et al. J Am Acad Dermatol. 2022;S0190-9622 [online ahead of print].
2. Armstrong AW, et al. [poster] Presented at the American Academy of Dermatology Annual Meeting, March 25–29, 2022, Boston, MA.
3. Armstrong AW, et al. J Dermatolog Treat. 2017;28:200-205.
4. Bushmakin AG, et al. Qual Life Res. 2011;20:491-498.
5. Warren RB, et al. J Eur Acad Dermatol Venereol. 2021;35:450-457.
6. Blauvelt A, et al. J Manag Care Spec Pharm. 2021;27:84-94.

Acknowledgments

- This study was supported by Bristol Myers Squibb
- Medical writing and editorial assistance was provided by Eleanor Bush, MA, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb

Disclosures

- AWA: 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
- SHP, VP, PN, MJ: Employees of and may own stock options in Bristol Myers Squibb
- W-JW, VC: Employees of OPEN Health, which has received consulting fees from Bristol Myers Squibb
• Adjusted AUC comparisons between the 2 treatment arms were based on an analysis of covariance (ANCOVA).

Presented at the Fall Clinical Dermatology Conference; October 20—23, 2022; Las Vegas, NV. This poster may not be reproduced without written permission from the authors. Email for April Armstrong, MD, MPH: AprilArmstrong@post.harvard.edu

• To evaluate the cumulative clinical benefit of initiating with deucravacitinib vs apremilast from baseline to Week 52.

The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast.

This study determined the AUC using data at a patient level (responder status at each time point over 52 weeks). Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index (PASI) score by Week 24 continued with apremilast.

Patients were aged ≥18 years, with body surface area involvement ≥10%.

Region (United States, China, Japan, rest of the world [ROW]).

Coprimary efficacy endpoints were PASI 75 and static Physician Global Assessment (sPGA) 0/1.

Nonresponder imputation was used for missing data.

Deucravacitinib initiators arm:

- At Week 52, 46.3% of these patients achieved at least 75% improvement from baseline in PASI score (PASI 75).
- Deucravacitinib initiators spent ≈150% more time in therapeutic response over 1 year compared with apremilast initiators.

Results

Standardized average cumulative response, %

- Standardized average cumulative PASI 75 response over 52 weeks among patients initiating with deucravacitinib was 50.2% compared with 31.9% in patients initiating with apremilast (P < 0.001).
- The adjusted difference in AUC0–52wk was 990.66 (95% CI, 683.37–1297.95); Adjusted AUC0–52wk, % × weeks was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm.

Figure 2. Standardized adjusted AUC0–52wk: PASI 75

Figure 3 displays the standardized adjusted cumulative AUC for PASI 75 over 52 weeks.

Table 1. Cumulative clinical benefit of deucravacitinib versus apremilast effect over time

| Week 24 | Week 48 | Week 52 |
|--------|--------|--------|
| PASI 50, ≥50% improvement from baseline in Psoriasis Area and Severity Index score. | | |

Conclusions

- Initiating with deucravacitinib resulted in greater cumulative benefits over 52 weeks than initiating with apremilast.
- Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line offers greater cumulative benefits.

Acknowledgments

1. Armstrong AW, et al. J Am Acad Dermatol. 2022;S0190-9622 [online ahead of print].
2. Blauvelt A, et al. J Eur Acad Dermatol Venereol. 2021;27:84-94.
3. Bushmakin AG, et al. J Am Acad Dermatol. 2022;35:450-457.
4. Bushmakin AG, et al. J Am Acad Dermatol. 2022;64:633-640.
5. Hanifin JM, et al. J Am Acad Dermatol. 2022;87:1-13.
6. Li Y, et al. J Am Acad Dermatol. 2022;86:471-481.

Medical writing and editorial assistance was provided by Eleanor Bush, MA, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.