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ORIGINAL RESEARCH

Matching-Adjusted Indirect Comparison of the Long-Term Efficacy of Deucravacitinib Versus Adalimumab for Moderate to Severe Plaque Psoriasis

April W. Armstrong · Sang Hee Park · Vardhaman Patel · Malcolm Hogan · Wei-Jhih Wang · David Davidson · Viktor Chirikov

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ABSTRACT

Introduction: Deucravacitinib, an oral tyrosine kinase 2 (TYK2) inhibitor, is approved in the United States to treat adults with moderate-to-severe plaque psoriasis (PsO). This study compared the long-term efficacy of deucravacitinib and adalimumab using results from long-term extension (LTE) trials.

Methods: Open-label LTE trials were identified for an indirect treatment comparison (deucravacitinib: POETYK PSO-LTE [NCT04036435]; adalimumab: REVEAL extension [NCT00195676]). To ensure study design comparability, patients initially randomized to placebo and switched to deucravacitinib or adalimumab after week 16 were compared. The primary outcome was an ≥ 75% reduction in Psoriasis Area and Severity Index score (PASI 75) at week 112 postrandomization. Secondary outcomes were PASI 75 at week 52 and an ≥ 90% reduction in PASI score (PASI 90) at weeks 52 and 112. Missing PASI data were imputed. A matching-adjusted indirect comparison was conducted; individual patient-level data from POETYK PSO-LTE were reweighted to balance baseline characteristics with those from the REVEAL extension.

Results: Before reweighting, on average, patients in the POETYK PSO-LTE (N = 329) versus the REVEAL (N = 345) extension were older, had a lower body weight, received more prior systemic treatments, and had higher baseline PASI scores and week 16 placebo PASI 75 and PASI 90 response rates. Following reweighting, adjusted week 112 PASI 75 response rates were significantly higher for deucravacitinib versus adalimumab (67.2% vs. 54.0%; mean difference [95% CI], 13.2 [4.0–22.5] percentage points). Deucravacitinib had a numerically higher adjusted week 112 PASI 90 response rate (41.3% vs. 34.0%; mean difference [95% CI], 7.3 [−2.0 to 16.7] percentage points). The treatments had similar week 52 adjusted PASI 75 and PASI 90 response rates.

Conclusion: In this interim analysis, adults with moderate to severe PsO had higher long-term response rates at 2 years when treated with

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A. W. Armstrong
Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

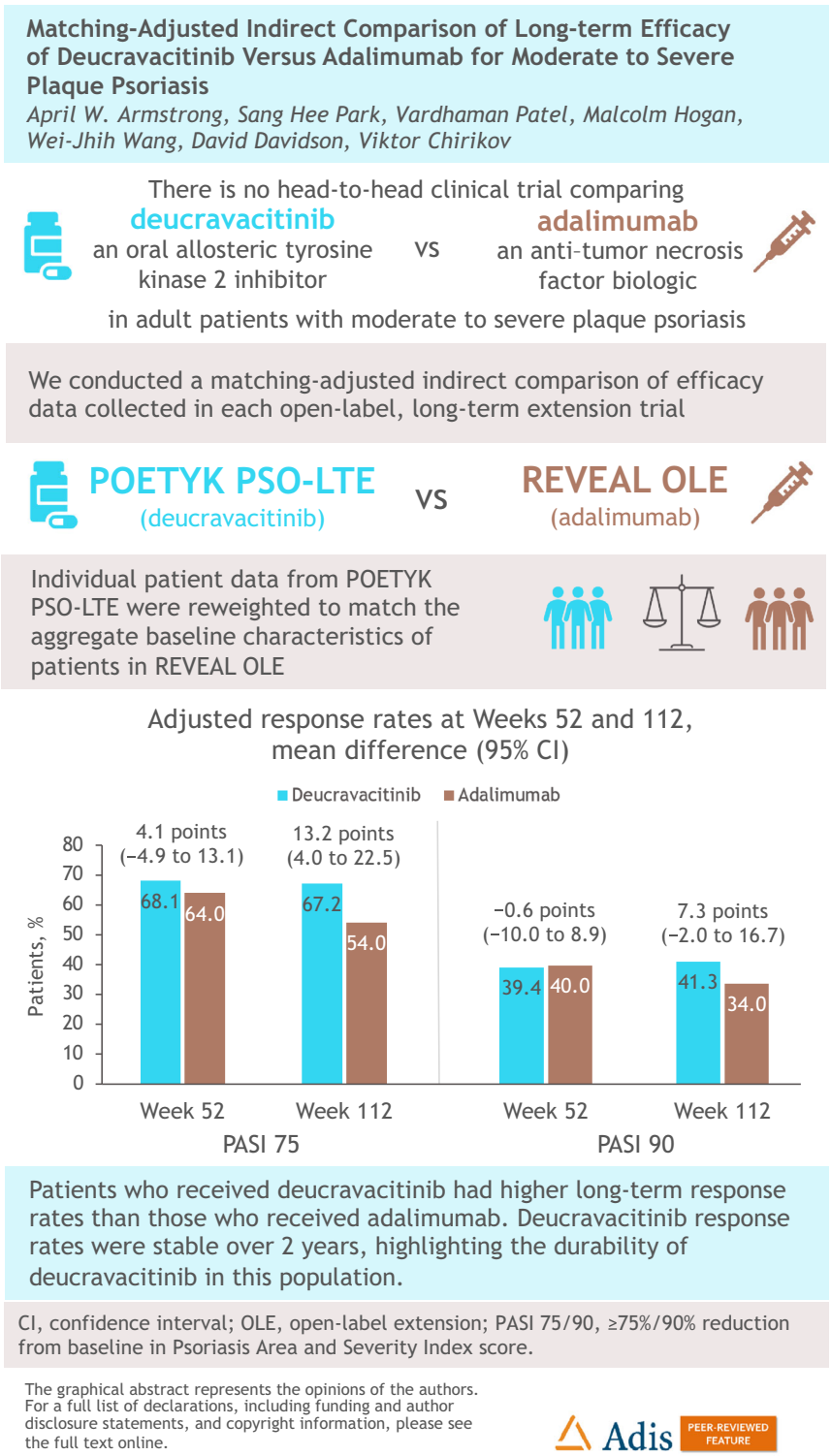
S. H. Park · V. Patel (✉) · D. Davidson
Bristol Myers Squibb, 3410 Princeton Pike, Princeton, NJ 08648, USA
e-mail: Vardhaman.patel@bms.com

M. Hogan
Syneos Health, Toronto, Canada

W.-J. Wang · V. Chirikov
OPEN Health Evidence & Access, Parsippany, NJ, USA

deucravacitinib versus adalimumab. Deucravacitinib response rates remained stable whereas adalimumab response rates declined in year 2.

Graphical Abstract:



PLAIN LANGUAGE SUMMARY

Plaque psoriasis is an inflammatory disease that causes red, itchy, dry patches (called plaques) on the skin. The disease cannot be cured, but the symptoms can be treated. Deucravacitinib and adalimumab are two treatments approved for use in adults with moderate to severe plaque psoriasis; deucravacitinib is an oral medication and adalimumab is injected with a needle under the skin. Each treatment has proven its efficacy compared with placebo (a pill or injection with no active effect) in separate clinical trials, but because no two clinical trials are exactly alike, the results cannot be accurately compared. Matching-adjusted indirect comparison is a method used to compare the results of one clinical trial with those of another when a direct comparison is not possible; characteristics from the patients in one trial are made to match the patient population in the other trial, and the adjusted results are compared. We performed a matching-adjusted indirect comparison of an open-label extension trial of deucravacitinib with an open-label extension trial of adalimumab to study the long-term efficacy of each treatment. At 1 year of treatment, we observed that similar proportions of patients receiving each treatment achieved a 75% or 90% improvement from their baseline Psoriasis Area and Severity Index score, called PASI 75 or PASI 90, respectively. At 2 years of treatment, similar proportions achieved PASI 90, but the proportion of patients receiving deucravacitinib who achieved PASI 75 was greater than that of patients receiving adalimumab.

Keywords: Adalimumab; Deucravacitinib; Indirect comparison; MAIC; Plaque psoriasis

Key Summary Points

Deucravacitinib, an oral allosteric tyrosine kinase 2 inhibitor, is approved in the United States, Europe, and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy.

Deucravacitinib demonstrated superior efficacy compared with apremilast and placebo in two phase 3 randomized controlled trials; in a previous network meta-analysis of clinical trial data, deucravacitinib showed comparable efficacy at 52 weeks to first-generation biologics, including adalimumab.

No head-to-head clinical trials have compared the long-term efficacies of deucravacitinib and adalimumab. Long-term extension trials were conducted for each drug, but differences in patient characteristics between the trial populations require adjustment for an appropriate comparison.

A matching-adjusted indirect comparison was conducted to assess long-term efficacy in adults with moderate to severe plaque psoriasis who switched from placebo to deucravacitinib or adalimumab at week 16 postrandomization and continued the respective treatment during a long-term extension trial.

Results from this interim analysis suggest that patients receiving deucravacitinib have a higher response rate than those receiving adalimumab at week 112.

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article, go to https://doi.org/10.6084/m9.figshare.23579091.

INTRODUCTION

Psoriasis is a chronic, immune-mediated, inflammatory skin disease that affects more than 7.5 million adults in the United States [1] and approximately 125 million individuals globally [2]. Plaque psoriasis (PsO) is the most common type of psoriasis, affecting approximately 80–90% of patients with psoriasis [3].

Systemic treatments used to treat moderate to severe PsO include nontargeted, nonbiologic agents (e.g., acitretin, methotrexate, and cyclosporine), targeted small molecules (apremilast and deucravacitinib), and biologic agents (e.g., tumor necrosis factor inhibitors [TNFis], interleukin [IL]-12/23 inhibitors, IL-17 inhibitors, and selective IL-23 inhibitors) [3]. Adalimumab, a TNFi, has been widely used to treat adults with moderate to severe PsO since its approval by the US Food and Drug Administration in 2008 [2, 4]. As new PsO therapies become available, including those administered orally, long-term efficacy and safety data as well as comparative data are needed to better understand the role of new therapies and their place in the existing PsO treatment landscape [5].

In September 2022, the US Food and Drug Administration approved deucravacitinib as a first-in-class, oral, allosteric tyrosine kinase 2 inhibitor for treatment of adults with moderate-to-severe PsO who are candidates for systemic therapy and phototherapy [6, 7]. The efficacy and safety of deucravacitinib in adults with moderate to severe PsO were demonstrated in the phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) registrational trials [8, 9]. Deucravacitinib administered once daily demonstrated superior efficacy in both trials compared with placebo and with apremilast across a variety of primary and secondary prespecified endpoints [8, 9]. After 52 weeks, patients completing the POETYK PSO-1 and PSO-2 trials could enroll in the POETYK PSO long-term extension (LTE) study to receive open-label deucravacitinib 6 mg once daily. In the POETYK PSO-LTE (NCT04036435) study, clinical efficacy was maintained for up to 2 years in patients treated with deucravacitinib, regardless of the treatment received at week 52 in the POETYK PSO-1 or PSO-2 trials [10].

Comparable efficacy was shown for deucravacitinib and some of the most effective first-generation biologics, including adalimumab, over 52 weeks in a previous systematic literature review and network meta-analysis [11]. However, the longer-term efficacy of deucravacitinib versus that of first-generation biologics is unknown. In lieu of results from head-to-head clinical trials comparing deucravacitinib with adalimumab in adults with moderate to severe PsO, a matching-adjusted indirect comparison (MAIC) was performed to compare long-term clinical outcomes with these agents. This paper aims to inform clinical practice by comparing long-term efficacy outcomes between a novel and an established treatment for PsO using a methodologically rigorous analytic technique.

METHODS

Patient Population

The POETYK PSO-LTE study was the data source used in this MAIC for individual patient-level data for deucravacitinib [10]. The population of interest was patients with moderate to severe PsO who, during the registrational studies (POETYK PSO-1 and PSO-2), received placebo from baseline to week 16, then crossed over in a blinded manner to receive deucravacitinib 6 mg once daily through week 52, and continued on deucravacitinib in the open-label POETYK PSO-LTE study. Patients treated with adalimumab prior to enrolling in the POETYK PSO-1 and PSO-2 studies were excluded from this analysis.

The comparator arm for this MAIC was identified from the REVEAL long-term open-label extension (OLE) study (NCT00195676) [12]. Specifically, the comparator arm for this

analysis comprised patients in the REVEAL OLE study who crossed over from blinded treatment with placebo to receive open-label adalimumab 40 mg every other week at week 16 of REVEAL and throughout the OLE, designated as group D in the OLE study.

Both the REVEAL OLE and the POETYK PSO-LTE studies reported PASI 75 and PASI 90 (i.e., $\geq$ 75% and $\geq$ 90% reductions from baseline in Psoriasis Area and Severity Index [PASI] scores) over the long term (Fig. 1). Group D from the REVEAL OLE study included 319 patients who did not achieve PASI 75 while receiving placebo and entered the OLE directly at week 16, plus an additional 26 patients who achieved PASI 75 while receiving placebo and continued to receive open-label adalimumab in the registrational trial before entering the OLE. Additional cohorts (groups A, B, and C) in the REVEAL OLE study did not have comparable counterparts in the POETYK PSO-LTE study, as the REVEAL and POETYK parent trials had different switching rules and different prespecified time points for implementing those rules. As the registrational trials for deucravacitinib and adalimumab were conducted more than a decade apart, with the POETYK trials beginning in 2018 [8, 9] and the REVEAL trial in 2004 [13], patients were excluded from the REVEAL trial for prior TNFi use; however, patients with prior TNFi use (other than adalimumab) were not specifically excluded from the POETYK PSO-LTE population used to conduct this MAIC.

Study Design

The study design was an unanchored MAIC (i.e., a comparison without a common comparator [14]) using individual patient-level data for deucravacitinib from the POETYK PSO-LTE study (i.e., pooled data from the POETYK PSO-1 and PSO-2 trials) and published aggregate data (e.g., baseline characteristics and outcomes) for adalimumab from group D of the REVEAL OLE study. See the Supplementary Materials Appendix for a detailed description of unanchored MAICs [14].

Outcomes

In patients with PsO, the PASI can be used to measure disease severity and the extent of disease involvement [15]. The primary outcome compared in this MAIC was PASI 75 at week 112 postrandomization. Secondary outcomes included PASI 75 at week 52 and PASI 90 at weeks 52 and 112 postrandomization. PASI scores at baseline assessment in the registrational studies were used to assess PASI 75 and PASI 90 responses. PASI 75 and PASI 90 endpoints between weeks 52 and 112 were also visually plotted for contextualization of the study results.

Statistical Analysis

Patients treated with deucravacitinib in POETYK PSO-LTE were reweighted to match the mean values of baseline characteristics of interest reported for the REVEAL OLE study, using the method of moments described by Signorovitch et al. [16, 17]. This approach generated population-adjustment weights for patients treated with deucravacitinib and balanced their baseline characteristics with those for patients treated with adalimumab. See the Supplementary Materials Appendix for a detailed description of the adjustment methodology [14, 17, 18]. The weighted mean difference in response rates with 95% confidence intervals (CIs), constructed via robust standard errors, were reported before and after adjusting for baseline characteristics for the two populations. Missing PASI response data from POETYK PSO-LTE were imputed using the last observation carried forward (LOCF) method to be consistent with how results were reported for adalimumab in the REVEAL OLE publication. The selection of variables to adjust was based on a review of patient characteristics known to be prognostic of response and/or systemic treatment effect modifiers as well as clinical guidance; the choice of patient characteristics used for adjustment in prior published MAICs was also considered [19–23].

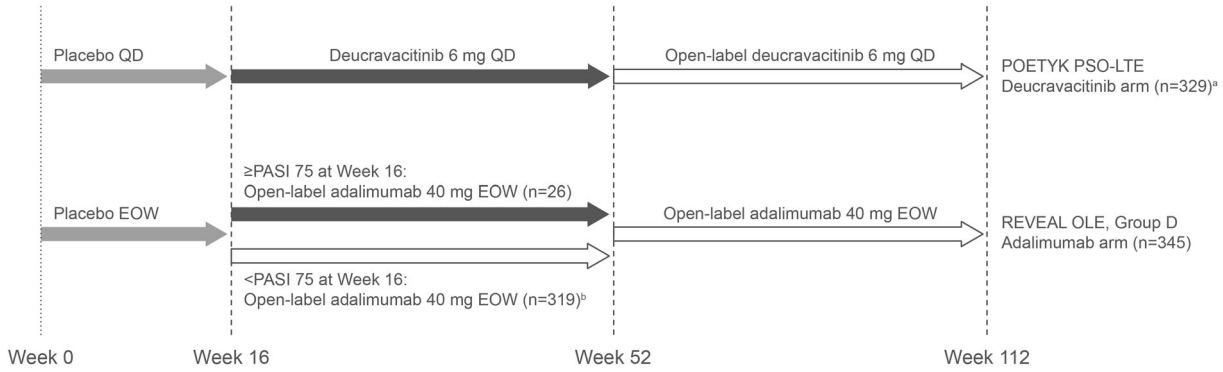


Fig. 1 POETYK and REVEAL study designs for the included comparator groups. [a]Excluding patients with prior adalimumab treatment. [b]In the REVEAL trial, patients with < PASI 75 at week 16 entered the open-label adalimumab arm. *EOW* every other week; *PASI 75* ≥ 75% improvement from baseline in Psoriasis Area and Severity Index score; *QD* once daily

Base Case

In the base case, the deucravacitinib cohort was adjusted for age, sex, race, weight, PsO duration, baseline body surface area involvement, baseline PASI score, placebo PASI 75 and 90 response rates at week 16 postrandomization, and prior use of phototherapy, systemic nonbiologic therapy, and systemic biologic therapy.

Sensitivity Analyses

Several sensitivity analyses were conducted. In sensitivity analysis 1, a history of psoriatic arthritis and the Physician Global Assessment score were added to the variables applied to the base case. In sensitivity analysis 2, previous use of phototherapy, systemic nonbiologic therapy, and systemic biologic therapy were not considered for adjustment as a modification to the base case to explore the effects of prior treatment and because the treatment landscapes were very different when the two studies were conducted. In sensitivity analysis 3, the treatment history for the POETYK population was limited to the prior 12 months, as in the REVEAL study. Truncation of weights was considered for any sensitivity analysis if indicated by the occurrence of extreme weights. In sensitivity analysis 4, the impact of extreme weights generated in the base case was tested by truncating weights at the 1% and 99% cutoff points of their distribution.

Compliance with Ethics Guidelines

This study did not require institutional review board approval as it did not access identifiable private information or have direct interaction/intervention with patients. This MAIC utilized data from previously conducted studies and did not contain data from any new studies with human participants or animals performed by any of the authors. Both studies examined were conducted in accordance with the principles of the Declaration of Helsinki, all study sites received approval from independent ethics committees, and all participants in the studies provided their informed consent. Aggregate data from the REVEAL study are publicly available and the authors had permission to access the patient-level data from the POETYK PSO-LTE study.

RESULTS

Demographics and Baseline Characteristics

Prior to reweighting, the POETYK PSO-LTE cohort included 329 patients and the REVEAL OLE cohort included 345 patients. Twenty-eight patients were excluded from the POETYK PSO-LTE cohort because they had received adalimumab prior to enrolling in the POETYK PSO-1

and PSO-2 studies. There were differences between the POETYK PSO-LTE and REVEAL OLE cohorts, respectively, in age (mean, 47.6 vs. 45.3 years), body weight (mean, 89.9 vs. 94.9 kg), and race (White, 85.4% vs. 91.3%). A greater proportion of patients in the POETYK PSO-LTE than in the REVEAL OLE studies previously received systemic nonbiologic (44.7% vs. 20.0%) or biologic (29.5% vs. 13.9%) PsO treatment. Fewer patients in the POETYK PSO-LTE than in the REVEAL OLE group D cohort had previously used topical therapy (30.1% vs. 71.9%). More patients in the POETYK PSO-LTE than in the REVEAL OLE studies achieved PASI 75 (13.4% vs. 7.0%) or PASI 90 (4.3% vs. 2.0%) post-placebo at week 16 (Table 1).

Unadjusted Outcomes Comparison

Prior to adjusting for differences in baseline characteristics, PASI 75 response rates were higher for deucravacitinib versus adalimumab at week 112 (71.7% vs. 54.0%; mean difference [95% CI], 17.7 percentage points [10.6–24.9]) and week 52 (69.9% vs. 64.0%; mean difference [95% CI], 5.9 percentage points [− 1.2 to 13.0]). PASI 90 response rates were also higher for deucravacitinib versus adalimumab at week 112 (46.8% vs. 34.0%; mean difference [95% CI], 12.8 percentage points [5.5–20.2]) and week 52 (42.9% vs. 40.0%; mean difference [95% CI], 2.9 percentage points [− 4.6 to 10.3]; Supplemental Table 1).

Adjusted Outcomes Comparison: Base Case

Following reweighting (Supplemental Fig. 1), most patient baseline demographics and disease characteristics were balanced between the REVEAL OLE and POETYK PSO-LTE studies (Table 1). The effective sample size (ESS) for the POETYK PSO-LTE population was 147 patients after adjustment.

After reweighting, the PASI 75 response rate was significantly higher for deucravacitinib at week 112 compared with adalimumab (67.2% vs. 54.0%), for a mean difference of 13.2 percentage points (95% CI 4.0–22.5; Fig. 2). Deucravacitinib had numerically higher PASI 90 response rates at week 112 compared with adalimumab (41.3% vs. 34.0%; mean difference [95% CI], 7.3 percentage points [− 2.0 to 16.7]). Adjusted PASI 75 (Fig. 2) and PASI 90 (Fig. 3) response rates at week 52 were comparable for the two treatments.

Adjusted Outcomes Comparison: Sensitivity Analyses

Demographics and baseline characteristics for the POETYK PSO-LTE cohort in the sensitivity analyses are presented in Table 2. Additional adjustment for Physician Global Assessment score and history of psoriatic arthritis further reduced the ESS for sensitivity analysis 1 (N = 86; Supplemental Fig. 2A, B), despite the truncation of extreme weights at the 1% and 99% percentiles. Distributions of adjustment weights without truncation for sensitivity analyses 2 and 3 are presented in Supplemental Fig. 2C, D. In contrast, truncation of extreme weights of the base case adjustment in sensitivity analysis 4 largely retained the balance in adjusted baseline characteristics, with a slight improvement in the ESS (N = 150; Supplemental Fig. 2E).

Overall, results from the sensitivity analyses were similar to those for the base case. PASI 75 response rates were significantly higher with deucravacitinib than adalimumab at week 112 (Fig. 4), with comparable response rates at week 52. PASI 90 response rates were numerically higher at week 112 for deucravacitinib versus adalimumab (Supplemental Fig. 3), while PASI 90 rates at week 52 were similar for the two treatments.

DISCUSSION

This MAIC compared the long-term efficacy of deucravacitinib versus that of adalimumab in adults with moderate to severe PsO using a well-established, rigorous analytic method. Results from the base case analysis showed that, following an adjustment for differences in baseline patient characteristics, adults with moderate to severe PsO treated with deucravacitinib had a

Table 1 Demographics and baseline characteristics for the POETYK PSO-LTE and REVEAL OLE cohorts before and after matching: base case

	Adalimumab REVEAL OLE group D (N = 345)	Deucravacitinib POETYK PSO-LTE	
		Unadjusted (N = 329)	Adjusted (ESS = 147)[a]
Age,[b] mean (SD), y	45.3 (13.2)	47.6 (14.1)	45.3 (13.9)
Male, %	67.0	70.2	67.0
White,[b] %	91.3	85.4	91.3
Weight,[b] mean (SD), kg	94.9 (22.6)	89.9 (20.5)	94.9 (22.4)
Duration of PsO, mean (SD), y	18.6 (11.8)	18.7 (13.0)	18.6 (16.6)
History of psoriatic arthritis, %	27.8	15.8	14.4
BSA, mean (SD)	25.5 (14.6)	25 (15.4)	25.5 (16.4)
PASI score,[b] mean (SD)	18.8 (7.1)	20.6 (8.0)	18.8 (6.7)
PGA,[b] %			
Moderate	55.7	83.3	87.3
Severe	44.3	16.7	12.7
Previous psoriasis treatment, %			
Phototherapy[b]	13.6[c]	38.9[d]	13.6[d]
Systemic nonbiologic[b]	20.0[c]	44.7[d]	20.0[d]
Systemic biologic[b]	13.9[c]	29.5[d]	13.9[d]
Post-placebo PASI 75 at week 16,[b] %	7.0	13.4	7.0
Post-placebo PASI 90 at week 16,[b] %	2.0	4.3	2.0

BSA body surface area; *ESS* effective sample size; *PASI* Psoriasis Area and Severity Index; *PASI 75* $\geq$ 75% improvement from baseline in PASI score; *PASI 90* $\geq$ 90% improvement from baseline in PASI score; *PGA* Physician Global Assessment; *PsO* plaque psoriasis; *SD* standard deviation

[a]Effective sample size after reweighting; baseline characteristics adjusted for age, sex, race, weight, duration of PsO, baseline body surface area, baseline PASI, previous use of phototherapy/systemic nonbiologic/systemic biologic therapy, and placebo PASI 75 and 90 response rates at week 16 postrandomization

[b]$P < 0.05$ for prematch comparisons between POETYK PSO-1 and 2 and REVEAL using t tests for continuous variables and chi-square tests for categorical variables

[c]Baseline capture defined as the 12 months prior to study initiation

[d]Baseline capture defined as any point in time in the treatment history

significantly higher PASI 75 response rate at week 112 compared with those treated with adalimumab. In sensitivity analyses evaluating the effects of potentially relevant clinical characteristics, results generally confirmed the base case results. Prior use of topical therapy was the only baseline characteristic from the REVEAL study not included in the matching adjustment. However, prior use of topical therapy was deemed not clinically important for the MAIC because patients included in this analysis were initially treated with placebo during the registrational studies, resulting in a 16-week washout period. In addition, there were limited nontopical treatment options available to treat PsO at the time of the REVEAL study, so more

than twice as many patients in the REVEAL group D versus POETYK PSO-LTE cohorts had prior use of topical therapy (71.9% vs. 30.1%), whereas more treatment options were available when the POETYK PSO-LTE study was conducted.

Results from a prior network meta-analysis demonstrated that oral deucravacitinib had comparable efficacy to adalimumab over 52 weeks [11], consistent with the results of our study at the same time point. In addition, results from this MAIC suggest that efficacy with deucravacitinib was maintained, as response rates were consistently higher with continuous deucravacitinib than with adalimumab from weeks 52 through 112. Our study results may be similar to those observed in a previous study that showed that patients may experience a loss of efficacy with biologic therapy over time [24]. Biologic therapies are large proteins with complex structures. There is a risk of these large, complex structures being recognized by the patient's immune system as foreign bodies that may elicit an immune response and the production of antidrug antibodies. This host immune response may be responsible for downstream effects, which include secondary nonresponse [25].

Although this study adjusted for the patient characteristics reported in both trials, no two trials are exactly alike; outcomes for this MAIC are subject to a higher level of uncertainty than would occur in a head-to-head randomized controlled trial comparing deucravacitinib and adalimumab. The adjustment to the published adalimumab data was based on aggregate proportions of patient characteristics but did not necessarily control for the joint distribution between characteristics associated with each individual patient. Therefore, associations between outcomes and baseline factors at the study level may be different than they would have been at the patient level. This MAIC was based on an interim data analysis for the POETYK PSO-LTE study; once the extension study has been completed, a data refresh will be warranted. The REVEAL OLE results were reported as full integers without decimal places, most likely for better clinical interpretability, so they may not represent the true values.

As an indirect comparison evaluates previously published data, differences in study design, such as when a patient enters the open-label portion of a study, could not be controlled. In the POETYK trials, patients remained blinded to treatment from weeks 16 to 52, whereas patients in the REVEAL trials received open-label treatment during the same period. However, data suggest that the absence of blinding (i.e., open-label versus blinded treatment) has little effect on perceived drug efficacy or on the outcome reporting rate [26].

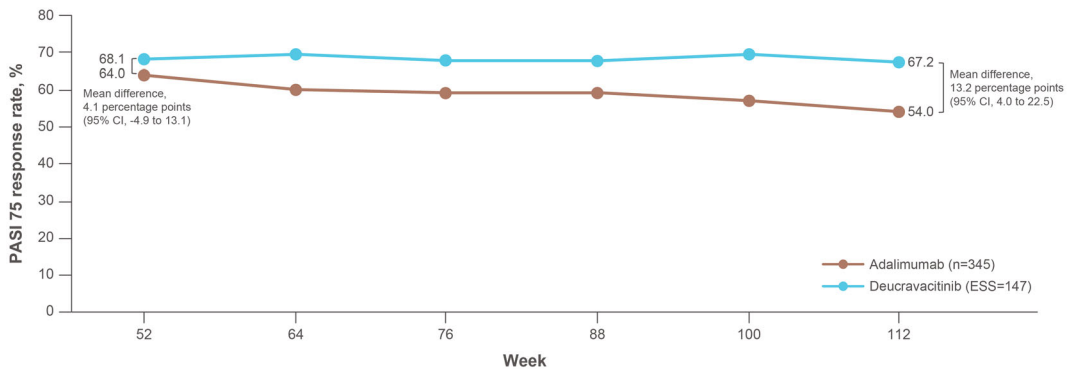


Fig. 2 Base case results: adjusted PASI 75 response rates at weeks 52 and 112 for deucravacitinib and adalimumab.[a] [a]Adjusted for age, sex, race, weight, duration of PsO, baseline body surface area, baseline PASI, previous use of phototherapy/systemic nonbiologic/systemic biologic therapy, and PASI 75/90 response post-placebo at week 16 postrandomization. *CI* confidence interval; *ESS* effective sample size; *PASI 75* $\geq$ 75% reduction from baseline in Psoriasis Area and Severity Index score

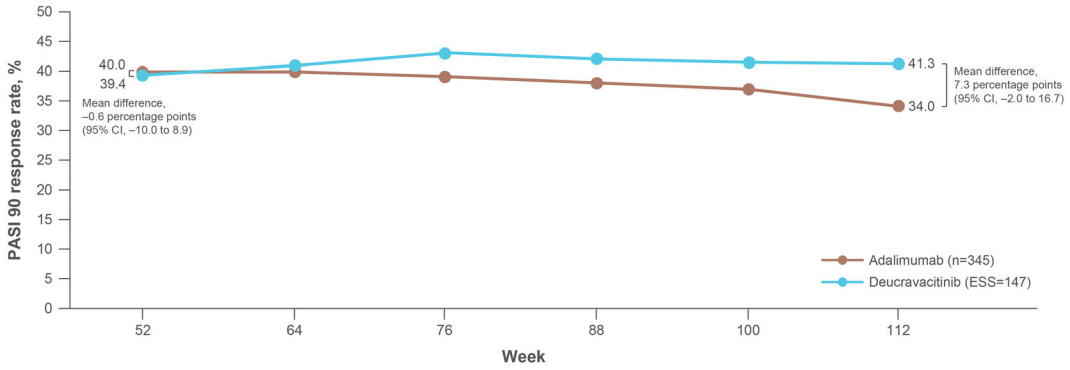


Fig. 3 Base case results: adjusted PASI 90 response rates at weeks 52 and 112 for deucravacitinib and adalimumab.[a] [a]Adjusted for age, sex, race, weight, duration of psoriasis, baseline body surface area, baseline PASI, previous use of phototherapy/systemic nonbiologic/systemic biologic therapy, and PASI 75/90 response post-placebo at week 16 postrandomization. *CI* confidence interval; *ESS* effective sample size; *PASI 90* $\geq$ 90% reduction from baseline in Psoriasis Area and Severity Index score

The POETYK and REVEAL trials were conducted more than a decade apart [8, 9, 13]. During this time, the treatment landscape for PsO expanded and patients gained access to novel treatments with various mechanisms of action [5]. Patients enrolled in the POETYK trials may have had a more diverse treatment history than those in the REVEAL trials owing to the approval and availability of new medications from 2004 to 2018. Additionally, previous treatment exposure in the REVEAL trial was limited to the 12 months prior to study initiation [12]. Conversely, previous systemic treatment exposure in the POETYK trials was not restricted to the 12 months prior to study initiation [8, 9]. Thus, it is not surprising that a greater proportion of patients in the POETYK PSO-LTE than in the REVEAL OLE studies previously received systemic nonbiologic or biologic PsO treatment. As few biologic therapies were approved before 2004, when the REVEAL trial was initiated (i.e., alefacept [later withdrawn], etanercept, efalizumab [later withdrawn], and infliximab), with many more recent biologic treatments available by the time the POETYK studies were initiated, we opted to keep the different capture periods for the POETYK and REVEAL trials for the base case analysis. The impact of this difference in definitions was explored in sensitivity analyses, which did not alter the main conclusions. Although patients were excluded from the REVEAL trial for prior TNFi use, we did not exclude patients with prior TNFi use (other than adalimumab) from the POETYK PSO-LTE population whose data were used to conduct this MAIC. Overall, the methodologic issue of a heterogeneous treatment history is mitigated by evidence from the POETYK trials demonstrating that prior biologic therapy is not prognostic of response to deucravacitinib [27]. Additionally, we adjusted for the placebo response after week 16, which should be considered as an all-inclusive composite measure of patients' likelihood to respond to future treatments.

We also examined the impact of using LOCF imputation on missing PASI 75 and PASI 90 values in the POETYK PSO-LTE study by comparing imputed values to the values obtained from patients with complete response data. We observed that the estimates obtained from patients with complete response data were higher than the estimates obtained using an LOCF approach. It is possible that the response estimates obtained using data from patients with complete response data were overestimated, as they represent patients with longer treatment durations; therefore, using the LOCF-imputed values is a more conservative approach. Moreover, the LOCF approach is consistent with the REVEAL OLE study analysis [12].

Table 2 Demographic and baseline characteristics for the POETYK PSO-LTE and REVEAL OLE cohorts: sensitivity analyses

	Adalimumab REVEAL OLE: group D (N = 345)	Deucravacitinib Adjusted POETYK PSO-LTE			
		Sensitivity analysis 1 (ESS = 86)[a,b,c]	Sensitivity analysis 2 (ESS = 238)[b,d]	Sensitivity analysis 3 (ESS = 221)[b,e]	Sensitivity analysis 4 (ESS = 150)[a,b,f]
Age, mean (SD), y	45.3 (13.2)	45.1 (12.3)	45.3 (13.9)	45.3 (13.8)	45.4 (13.9)
Male, %	67.0	65.2	67.0	67.0	67.4
White, %	91.3	90.8	91.3	91.3	91.2
Weight, mean (SD), kg	94.9 (22.6)	94.6 (21.3)	94.9 (21.9)	94.9 (22.1)	94.7 (22.4)
Duration of PsO, mean (SD), years	18.6 (11.8)	19.0 (14.3)	18.6 (13.0)	18.6 (12.8)	18.6 (13.7)
History of psoriatic arthritis, %	27.8	29.4	14.3	13.9	14.5
BSA, mean (SD)	25.5 (14.6)	25.0 (15.1)	25.5 (16.3)	25.5 (16.1)	25.5 (16.4)
PASI, mean (SD)	18.8 (7.1)	18.8 (6.6)	18.8 (6.5)	18.8 (6.5)	18.8 (6.8)
PGA, %					
Moderate	55.7	58.9	87.8	88.6	87.2
Severe	44.3	41.1	12.2	11.4	12.8
Previous PsO treatment, %					
Phototherapy	13.6	14.4	39.6	13.6	13.7
Systemic nonbiologic	20.0	21.1	44.7	20.0	20.1
Systemic biologic	13.9	14.7	29.3	13.9	14.0
Post-placebo PASI 75 at week 16, %	7.0	7.4	7.0	7.0	7.0
Post-placebo PASI 90 at week 16, %	2.0	2.1	2.0	2.0	2.0

BSA body surface area; *PASI* Psoriasis Area and Severity Index; *PASI 75* $\geq$ 75% improvement from baseline in PASI score; *PASI 90* $\geq$ 90% improvement from baseline in PASI score; *PGA* Physician Global Assessment; *PsO* plaque psoriasis; *SD* standard deviation

[a]Results were truncated at 1% and 99% owing to extreme weights

[b]Effective sample size after reweighting

[c]Sensitivity analysis 1: base-case variables adjustment with history of psoriatic arthritis and PGA added

[d]Sensitivity analysis 2: base-case variables adjustment with prior treatment history (i.e., phototherapy/systemic nonbiologic/systemic biologic therapy) removed

[e]Sensitivity analysis 3: base-case variables adjustment with treatment history limited to the 12 months prior to study initiation

[f]Sensitivity analysis 4: base-case variables adjustment with truncation of extreme weights

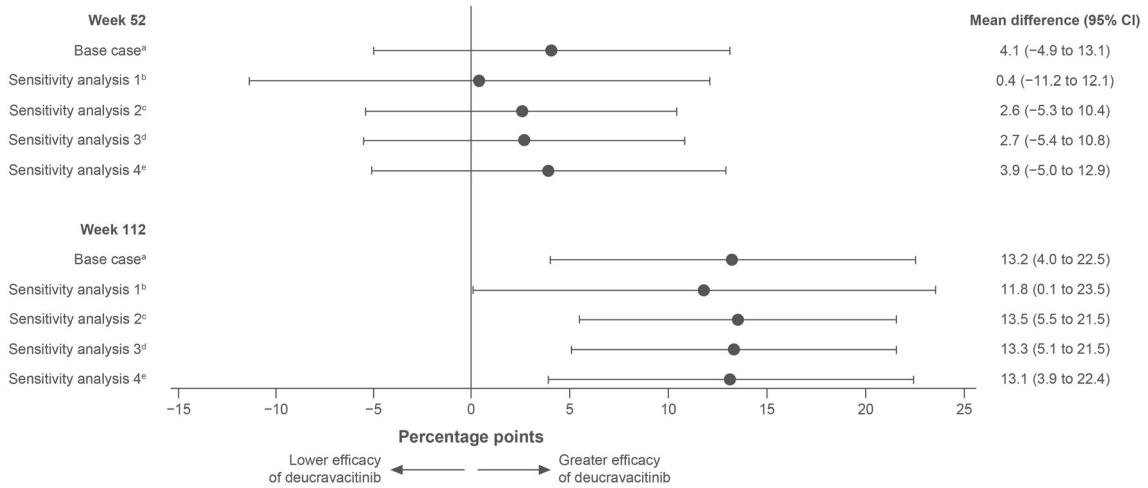


Fig. 4 Base case and sensitivity analyses: mean difference in adjusted PASI 75 response rates at weeks 52 and 112 between deucravacitinib and adalimumab. [a]Base case adjusted for age, sex, race, weight, duration of psoriasis, baseline body surface area, baseline PASI, previous use of phototherapy/systemic nonbiologic/systemic biologic therapy, and PASI 75/90 response post-placebo at week 16 postrandomization. Adalimumab, N = 345; deucravacitinib, ESS = 147. [b]Sensitivity analysis 1: base-case variables adjustment with history of psoriatic arthritis and PGA added. Adalimumab, N = 345; deucravacitinib, ESS = 86. [c]Sensitivity analysis 2: base-case variables adjustment with prior treatment history (i.e., phototherapy/systemic nonbiologic/systemic biologic therapy) removed. Adalimumab, N = 345; deucravacitinib, ESS = 238. [d]Sensitivity analysis 3: base-case variables adjustment with treatment history limited to the 12 months prior to study initiation. Adalimumab, N = 345; deucravacitinib, ESS = 221. [e]Sensitivity analysis 4: base-case variables adjustment with truncation of extreme weights. Adalimumab, N = 345; deucravacitinib, ESS = 150. *CI* confidence interval; *ESS* effective sample size; *PASI 75* ≥ 75% reduction from baseline in Psoriasis Area and Severity Index score

As previously described, the trial design for both long-term efficacy analyses included patients who initiated treatment with placebo then switched to active treatment at week 16. Some cohorts in the REVEAL OLE study that were not used for this comparative analysis initiated treatment with adalimumab 80 mg, which was then tapered to 40 mg. Patients in these cohorts had higher response rates than patients from REVEAL group D, who were included as the comparator arm in this MAIC (i.e., patients who switched from placebo to adalimumab 40 mg at week 16) [4]. Further research may be needed to compare dose-specific response rates for deucravacitinib and adalimumab.

Several limitations that apply to any indirect comparison of published data should be acknowledged. As discussed above, the results of this study are subject to a higher level of uncertainty than what would occur in a head-to-head randomized, controlled trial, and differences in study design (e.g., open-label vs. blinded treatment) could not be controlled. There also may be different associations between outcomes and baseline factors at the study level than at the patient level.

CONCLUSION

Our study findings highlight the therapeutic role of deucravacitinib 6 mg once daily and illustrate its long-term effect versus adalimumab 40 mg every other week in patients with moderate to severe PsO. Adults with moderate to severe PsO treated with deucravacitinib versus adalimumab had higher long-term response rates at 2 years. Response rates for deucravacitinib also remained stable over time, whereas response rates for adalimumab declined in the second year. Patients with moderate to severe

PsO may benefit from oral treatment with deucravacitinib owing to its demonstrated long-term efficacy. Future research on the relationship between patient genetic profile and inadequate treatment response is recommended to help improve treatment decision making.

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Compliance with Ethics Guidelines This study did not require institutional review board approval as it did not access identifiable private information or have interaction/intervention with patients. This MAIC utilized data from previously conducted studies. Both of the studies examined were conducted in accordance with the principles of the Declaration of Helsinki, all study sites received approval from independent ethics committees, and all participants in the studies provided their informed consent. Aggregate data from the REVEAL study are publicly available and the authors had permission to access the patient-level data from the POETYK PSO-LTE study.

Data Availability The Bristol Myers Squibb policy on data sharing may be found at https://www.bms.com/researchers-and-partners/independent-research/data-sharing-request-process.html.

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