Matching-adjusted indirect comparison (MAIC) of deucravacitinib versus adalimumab for the treatment of patients with moderate to severe plaque psoriasis over 2 years

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Synopsis

- Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor that has demonstrated superior efficacy compared with apremilast and placebo in 2 phase 3 randomized controlled trials,[1,2] and is approved by the US Food and Drug Administration for the treatment of adults with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy
- A previous systemic literature review and network analysis indirectly compared the efficacy of deucravacitinib with other systemic nonbiologic and biologic treatments[3]
  - At Week 52, Psoriasis Area and Severity Index (PASI) response rates for deucravacitinib were comparable to those of the most effective first-generation biologics, including adalimumab
- A matching-adjusted indirect comparison (MAIC) evaluated the results of the adalimumab REVEAL trial vs those of the deucravacitinib POETYK PSO-1 and PSO-2 trials to extend the comparison beyond 52 weeks
- Among patients with moderate to severe PsO who switched from placebo to continuous treatment after Week 16, this MAIC suggests that patients receiving deucravacitinib had a higher long-term response rate than those receiving adalimumab
  - Response rates of at least 75% reduction from baseline in PASI scores (PASI 75) were significantly higher with deucravacitinib vs adalimumab at Week 112 and were numerically higher at Week 52
  - Response rates of at least 90% reduction from baseline in PASI scores (PASI 90) were similar between the 2 treatments at Week 52, but were numerically higher for deucravacitinib vs adalimumab at Week 112

Background

- POETYK PSO-1 and PSO-2
  - Randomized, double-blind, placebo-controlled studies assessing the efficacy and safety of deucravacitinib vs placebo and apremilast in adults with moderate to severe PsO
  - At Week 16, patients randomized to placebo crossed over to deucravacitinib
  - Patients completing PSO-1 and PSO-2 could enroll in a long-term, open-label extension during which patients received deucravacitinib 6 mg once daily
- A previous indirect comparison assessed the clinical efficacy associated with deucravacitinib and other selected active biologic and nonbiologic treatments[3]
  - The PASI 75 response rates were within the range of those for first-generation biologics at Weeks 10-16 and 24-28
  - At Week 52, the PASI 75 response rate for deucravacitinib was comparable to that of adalimumab and ustekinumab

Objective

- Primary objective
  - Compare the rates of PASI 75 response at Week 112 in patients with PsO treated with deucravacitinib vs adalimumab, adjusting for differences in baseline characteristics by using MAIC
- Secondary objective
  - Compare the rates of PASI 75 and PASI 90 response at Week 52 as well as the rate of PASI 90 response at Week 112, using MAIC, for patients treated with deucravacitinib vs adalimumab

Methods

- A literature search was conducted to identify long-term extension (LTE) trials that were similar to the design of the POETYK PSO-LTE and reported similar outcomes of interest (ie, PASI 75 and PASI 90 over the long term)

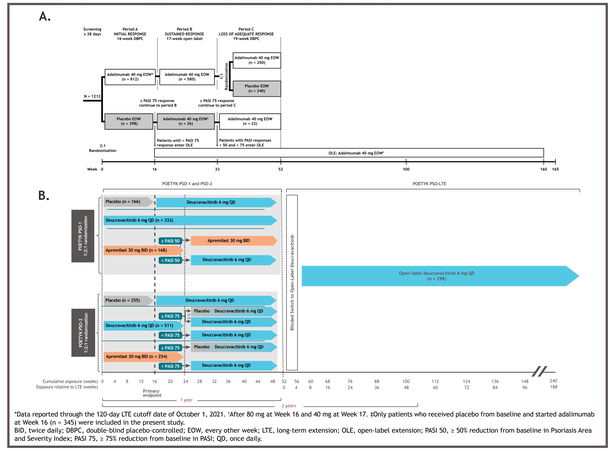
Adalimumab trial selection: REVEAL extension trial (NCT00195676)

- Randomized, double-blind, placebo-controlled study (**Figure 1A**) examining the clinical efficacy of adalimumab in patients with moderate to severe PsO
- Patients who did not achieve a PASI 75 response at Week 16 entered an open-label extension study of adalimumab
  - The long-term extension included the specific population of interest (patients with moderate to severe PsO), with a study design in which patients received continuous adalimumab over a long-term period
- Only patients initially randomized to placebo then switched to adalimumab at Week 16 were included in the MAIC
- Only published aggregate data were available[4]

Deucravacitinib trial selection: POETYK PSO-LTE (NCT04036435)

- Randomized, double-blind, placebo- and active-controlled phase 3 study with individual patient-level data available
- In both POETYK trials, patients with moderate to severe PsO were randomized to placebo and switched to deucravacitinib at Week 16 in an open-label, long-term extension (**Figure 1B**)
- Only patients initially randomized to placebo then switched to deucravacitinib were included in the MAIC, given the outcomes reported

Figure 1. Study design comparison between (A) REVEAL and (B) POETYK PSO-1 and PSO-2



*Data reported through the 120-day LTE cutoff date of October 1, 2021. †After 80 mg at Week 16 and 40 mg at Week 17. ‡Only patients who received placebo from baseline and started adalimumab at Week 16 (n = 345) were included in the present study.
BID, twice daily; DBPC, double-blind placebo-controlled; EOW, every other week; LTE, long-term extension; OLE, open-label extension; PASI 50, ≥ 50% reduction from baseline in Psoriasis Area and Severity Index; PASI 75, ≥ 75% reduction from baseline in PASI; QD, once daily.

Analyses

- **Base case:** age, sex, race, weight, duration of PsO, body surface area (BSA), baseline PASI score, previous use of phototherapy/systemic nonbiologics/systemic biologics, and Week 16 PASI 75/Week 16 PASI 90 scores
- **Sensitivity analysis 1:** history of psoriatic arthritis and Physician Global Assessment score, in addition to base case variables
- **Sensitivity analysis 2:** previous use of phototherapy/systemic nonbiologics/systemic biologics removed to only match on disease severity, demographics, and other baseline characteristics
- **Sensitivity analysis 3:** previous use of phototherapy/systemic nonbiologics/systemic biologics were limited to the prior 12 months only, to align with the definition used in REVEAL
- **Sensitivity analysis 4:** same as base case, with weight truncation allowed
- Truncation was conducted in sensitivity analyses if any extreme weights were observed

Outcome measures

- Primary outcome: PASI 75 response rate at Week 112
- Secondary outcomes: PASI 75 response rate at Week 52; PASI 90 response rate at Weeks 52 and 112
- Outcomes were analyzed using last observation carried forward (LOCF) to be consistent with the reported methods for REVEAL

Results

- Baseline characteristics
  - Before matching, patients in the POETYK studies were generally older, had higher mean baseline PASI scores, and were more likely to have been treated previously with systemic nonbiologic and biologic treatments compared with the patients in REVEAL (**Tables 1, 2**)

Table 1. Demographics and baseline characteristics before and after matching: base case

Parameter	REVEAL (N = 345)	POETYK prematch (N = 329)	POETYK postmatch (N = 147)[a]
Age, mean (SD), years	45.3 (13.2)	47.6 (14.1)	45.3 (13.9)
Male, %	67.0	70.2	67.0
White, %	91.3	85.4	91.3
Weight, mean (SD), kg	94.9 (22.6)	89.9 (20.5)	94.9 (22.4)
Duration of PsO, mean (SD), years	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, mean (SD)	18.8 (7.1)	20.6 (8.0)	18.8 (6.7)
PGA, %			
Moderate	55.7	83.3	87.3
Severe	44.3	16.7	12.7
Previous PsO treatment, %			
Phototherapy	13.6	38.9	13.6
Systemic nonbiologic	20.0	44.7	20.0
Systemic biologic	13.9	29.5	13.9
Week 16 PASI 75 response, %	7.0	13.4	7.0
Week 16 PASI 90 response, %	2.0	4.3	2.0

[a]Effective sample size after reweighting.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PsO, psoriasis; SD, standard deviation.

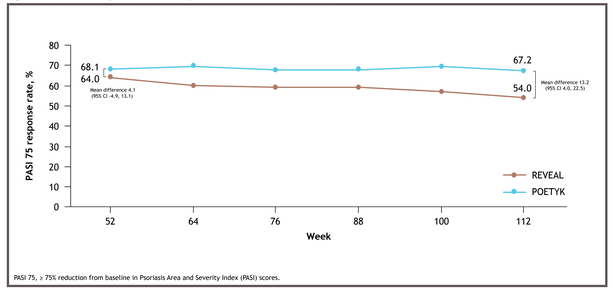
Table 2. Demographics and baseline characteristics: sensitivity analyses

Parameter	REVEAL (N = 345)	Sensitivity analysis 1[a] (n = 86)	Sensitivity analysis 2 (n = 238)	Sensitivity analysis 3 (n = 221)	Sensitivity analysis 4 (n = 150)
Age,[b] mean (SD), years	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,[b] %	91.3	90.8	91.3	91.3	91.2
Weight,[b] 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,[b] mean (SD)	18.8 (7.1)	18.8 (6.6)	18.8 (6.5)	18.8 (6.5)	18.8 (6.8)
PGA,[b] %					
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[b]	13.6	14.4	39.6	13.6	13.7
Systemic nonbiologic[b]	20.0	21.1	44.7	20.0	20.1
Systemic biologic[b]	13.9	14.7	29.3	13.9	14.0
Week 16 PASI 75[b] response, %	7.0	7.4	7.0	7.0	7.0
Week 16 PASI 90[b] response, %	2.0	2.1	2.0	2.0	2.0

[a]Results were truncated at 1% and 99% owing to extreme weights. [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.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PsO, psoriasis; SD, standard deviation.

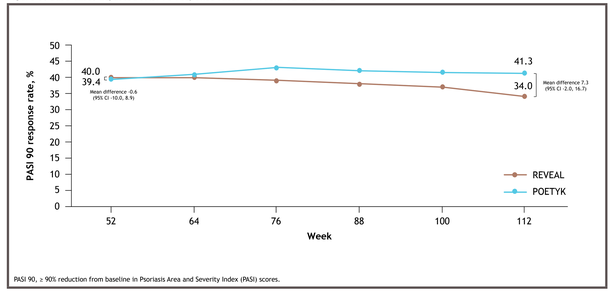
- Before matching
  - PASI 75 response rates were higher for deucravacitinib than adalimumab at Weeks 52 (69.9% vs 64.0%) and 112 (71.7% vs 54.0%)
  - Similarly, PASI 90 response rates were higher for deucravacitinib than adalimumab at Week 52 (42.9% vs 40.0%) and Week 112 (46.8% vs 34.0%)
- After matching
  - PASI 75 response rate was significantly higher for deucravacitinib at Week 112 compared with adalimumab (**Figure 2**), with a mean difference of 13.2% (95% confidence interval [CI], 4.0-22.5)
  - Deucravacitinib had numerically higher PASI 75 response rates at Week 52 and PASI 90 response rates at Week 112 compared with adalimumab, and PASI 90 response rates were comparable at Week 52 (**Figure 3**)
- Similar results were seen in the sensitivity analyses
  - PASI 75 response rate was significantly higher for deucravacitinib than adalimumab at Week 112 (**Figure 4**)
  - PASI 90 response rates were numerically higher at Week 112 for deucravacitinib vs adalimumab (**Figure 5**)
  - At Week 52, PASI 75 and PASI 90 response rates were comparable for deucravacitinib and adalimumab

Figure 2. Base case: adjusted PASI 75 response rates at Weeks 52 and 112



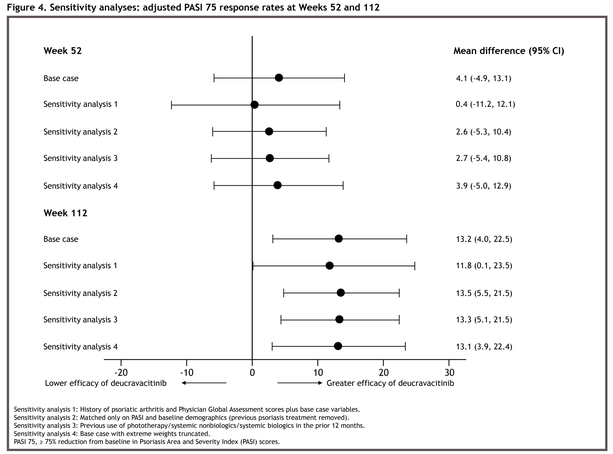
PASI 75, ≥ 75% reduction from baseline in Psoriasis Area and Severity Index (PASI) scores.

Figure 3. Base case: adjusted PASI 90 response rates at Weeks 52 and 112



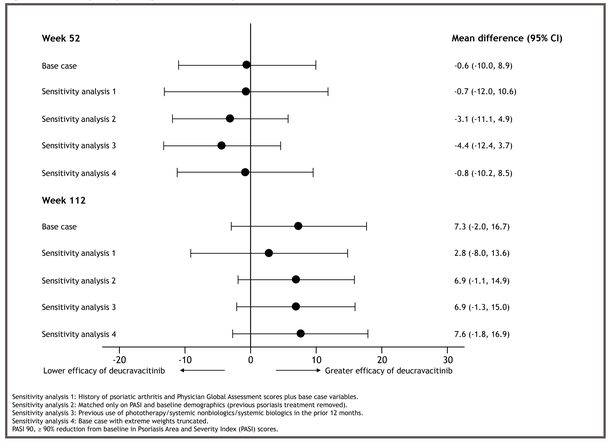
PASI 90, ≥ 90% reduction from baseline in Psoriasis Area and Severity Index (PASI) scores.

Figure 4. Sensitivity analyses: adjusted PASI 75 response rates at Weeks 52 and 112



Sensitivity analysis 1: History of psoriatic arthritis and Physician Global Assessment scores plus base case variables.
Sensitivity analysis 2: Matched only on PASI and baseline demographics (previous psoriasis treatment removed).
Sensitivity analysis 3: Previous use of phototherapy/systemic nonbiologics/systemic biologics in the prior 12 months.
Sensitivity analysis 4: Base case with extreme weights truncated.
PASI 75, ≥ 75% reduction from baseline in Psoriasis Area and Severity Index (PASI) scores.

Figure 5. Sensitivity analyses: adjusted PASI 90 response rates at Weeks 52 and 112



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Sensitivity analysis 3: Previous use of phototherapy/systemic nonbiologics/systemic biologics in the prior 12 months.
Sensitivity analysis 4: Base case with extreme weights truncated.
PASI 90, ≥ 90% reduction from baseline in Psoriasis Area and Severity Index (PASI) scores.

Conclusions

- Among patients with moderate to severe PsO who switched from placebo to continuous deucravacitinib treatment after Week 16, this MAIC suggests that patients who receive deucravacitinib have a greater long-term response rate than those who receive adalimumab
  - PASI 75 response rates were significantly higher with deucravacitinib vs adalimumab at Week 112 and were numerically higher at Week 52
  - PASI 90 response rates were comparable between the 2 treatments at Week 52, but were numerically higher for deucravacitinib at Week 112 compared with adalimumab
  - The sensitivity analyses showed similar results, with PASI 75 and 90 response rates with deucravacitinib being consistently higher than those for adalimumab at Week 112
- Limitations
  - Methodologies differed between the studies; differences in inclusion criteria and analyses may have affected these comparisons
  - Adjustments to published adalimumab data were based on aggregate proportions of patient characteristics and did not necessarily control for the joint distribution between characteristics associated with each individual patient
  - Associations between outcomes and baseline factors at the study level may be different than they would have been on the patient level, introducing potential uncertainty
- These results highlight the therapeutic role of deucravacitinib in PsO

References

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