Adv Ther (2025) 42:233–245
https://doi.org/10.1007/s12325-024-03034-1

ORIGINAL RESEARCH

# Comparative Effectiveness of Biologic Classes in Clinical Practice: Month 12 Outcomes from the International Observational Psoriasis Study of Health Outcomes (PSoHO)

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Received: August 13, 2024 / Accepted: October 10, 2024 / Published online: November 9, 2024


## ABSTRACT

***Introduction*:** Studies directly comparing the effectiveness of different biologics over long observation periods are lacking. As many treatment guidelines are formulated based on drug class, there is a particular need to compare drug classes rather than specific biologic agents.

***Methods*:** This post hoc analysis compares the effectiveness and durability of biologics that target the interleukin (IL)-17 A ligands or the IL-17 receptor A (IL-17RA) relative to other approved drug classes in patients with moderate-to-severe plaque psoriasis, through 12 months in a real-world setting.

***Results*:** In the Psoriasis Study of Health Outcomes (PSoHO) ($N = 1981$), patients treated with anti-IL-17A/RA resulted in a higher proportion of patients who achieved the primary outcome

**Prior Presentation**: A part of this work has previously been presented at the American Academy of Dermatology in San Diego, USA, in March (8–12) 2024.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s12325-024-03034-1.

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[proportion of patients who had at least a 90% improvement in Psoriasis Area and Severity Index score (PASI90) and/or a score of 0 or 1 in static Physician Global Assessment (sPGA)] compared to anti-IL-23-, anti-IL-12/23-, and tumor necrosis factor (TNF)-α-treated patients at week 12, month 6, and month 12, except versus anti-IL-23 at month 12. Similar trends were observed for a 100% improvement in PASI score (PASI100), PASI90, and Dermatology Life Quality Index score of 0 or 1 [DLQI (0,1)]. At month 12, the unadjusted response rates across the drug classes were 53.5–69.1% for the primary outcome, 27.6–40.8% for PASI100, 41.7–55.9% for PASI90, and 31.8–33.0% for DLQI (0,1). Regarding the durability of effectiveness, anti-IL-17A/RA patients had the highest response rate, and for the adjusted analysis, using Frequentist Model Averaging (FMA), patients had 1.4–2.6 times higher odds of achieving the primary durability outcome compared to patients treated with any other drug class.

***Conclusion***: Overall, anti-IL-17A/RA had the highest effectiveness of achieving early response to treatment and maintaining that response through 12 months compared to other drug classes.

***Trial Registration***: The study was registered at the European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCEPP24207).

**Keywords:** PSoHO; Psoriasis; IL-17A; PASI90; PASI100; DLQI; Biologic therapies

**Key Summary Points**

For moderate-to-severe plaque psoriasis (PsO) there is a lack of studies directly comparing the effectiveness of different biologics over long observation periods.

This post hoc analysis uses real-world data from the large, international, observational Psoriasis Study of Health Outcomes (PSoHO) study, and compares the effectiveness and durability of different drug classes through 12 months.

Biologics that target the interleukin (IL)-17 A ligands or the IL-17 receptor A (Anti-IL-17A/RA) showed a numerically higher response rate of achieving Psoriasis Area and Severity Index score (PASI) 90 and/or static Physician Global Assessment (sPGA) score of 0 or 1 at week 12, month 6, and month 12 compared to other drug classes, except for anti-IL-23 at month 12, with similar trends being observed for PASI100, PASI90, and Dermatology Life Quality Index score of 0 or 1 [DLQI (0,1)].

Regarding the achievement of response at week 12 and maintaining response at month 6 and 12, anti-IL-17A/RA patients displayed the highest numerical response rate.

For the adjusted analysis, using Frequentist Model Averaging (FMA), patients treated with anti-IL-17A/RA had 1.4–2.6 times higher odds of achieving the primary durability outcome compared to patients treated with any other drug class.

## INTRODUCTION

An improved understanding of psoriasis pathogenesis has led to the development of biologic therapies, which have transformed the treatment landscape for moderate-to-severe plaque psoriasis (PsO) [1–3]. Several classes of biologic agents are currently approved by the United States Food and Drug Administration (FDA) for use in PsO, namely, tumor necrosis factor (TNF)-α inhibitors (etanercept, adalimumab, infliximab, and certolizumab pegol), interleukin (IL)-12/23 p40 inhibitor (ustekinumab), IL-23 p19 inhibitors (guselkumab, tildrakizumab, and risankizumab) and, lastly, IL-17 inhibitors [4], which include biologics that target either the IL-17 ligands (IL-17A: secukinumab, ixekizumab;

IL17A/F: bimekizumab) or the IL-17 receptor A (IL-17RA: brodalumab) [5–7].

Many clinical studies primarily focus on comparing individual biologics, as there is substantial variability among therapies within each class; however, many treatment guidelines are formulated based on drug classes rather than specific biologic agents [8, 9]. By grouping biologics into classes, a structured and organized framework can be provided, thus allowing us to gain a better understanding of the broader therapeutic approach and comprehending the overall effects of blocking a specific pathway, both in terms of effectiveness and durability [10, 11].

The international, prospective Psoriasis Study of Health Outcomes (PSoHO) is a non-interventional cohort study and was designed to investigate the comparative effectiveness of biologic treatments for patients with moderate-to-severe plaque PsO in a real-world setting [12–15]. Building on previously published month 12 results of individual biologics from the PSoHO study, this manuscript aims to provide drug class-level data by categorizing individual biologics into distinct classes and to compare their effectiveness and durability of treatment responses.

## METHODS

### PSoHO Study Design

Briefly, PSoHO is an ongoing, 3-year, international, prospective, non-interventional cohort study. PSoHO reflects the treatment of patients with moderate-to-severe plaque PsO with biologics in a real-world setting. Details of the PSoHO study including eligibility criteria, baseline patient demographics, and clinical characteristics, as well as all prescribed biologics have been previously published [12, 13]. In this post hoc analysis, biologics targeting IL-17 was compared to other biologic classes.

For drug class analysis, drugs targeting the IL-17A ligand (IL-17A: ixekizumab, secukinumab) and the IL-17 receptor A (IL-17RA: brodalumab) were combined and reclassified from previous PSoHO studies to IL-17A/RA cohort as they block IL-17. The IL-17A/RA cohort was compared to TNFα (adalimumab, certolizumab, etanercept, and infliximab), IL-23 p19 (guselkumab, risankizumab, and tildrakizumab) and IL-12/23 p40 (ustekinumab) inhibitors. Although bimekizumab is now approved by the FDA [16] and EMA [17], PSoHO's enrollment was completed before its approval; therefore, no patients were prescribed bimekizumab at baseline.

### Study Endpoints

The outcomes analyzed in this study included the effectiveness, quality of life, and durability of effectiveness outcomes up to month 12 as previously described [13]. Effectiveness outcomes were assessed at week 12, month 6, and month 12 and included (1) primary outcome: patients who achieved at least a 90% improvement in the Psoriasis Area and Severity Index (PASI) score (PASI90) and/or static Physician Global Assessment (sPGA) score of 0 or 1 (sPGA 0/1), (2) patients who achieved PASI100, and (3) patients who achieved PASI90. Quality of life outcome was assessed at week 12, month 6, and month 12 for patients with a Dermatology Life Quality Index (DLQI) score of 2 or greater at baseline and subsequently achieved a DLQI score of 0 or 1 [DLQI (0, 1)]. The durability of effectiveness outcomes included (1) patients who met the primary outcome at week 12 and who subsequently at months 6 and 12, achieved at least PASI75 and/or 2 or more points in sPGA score from baseline, (2) patients who achieved PASI100 at week 12 and maintained at both month 6 and 12, and (3) patients who achieved PASI90 at week 12 and maintained at both month 6 and 12.

### Statistical Approach

The comparative effectiveness analyses were performed using a data-driven approach known as the Frequentist Model Averaging (FMA); an overview of this data-driven methodology including statistical appendixes has been described previously [12–14]. Unadjusted response rates are reported as proportions of patients reaching

each outcome. Comparative adjusted results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance is indicated by the 95% CIs not crossing the null hypotheses (OR = 1). For baseline characteristics, missing values for continuous variables were imputed as mean, and missing values for categorical variables were imputed as the most frequent class of categorical variables. Patients with missing binary outcomes were imputed by non-responder imputation (NRI). Baseline patient demographics and disease characteristics among drug classes are reported as mean and standard deviation for continuous variables and as number of patients and percentages for categorical variables. A further subgroup analysis focused on patients who received the United States (US) on-label dosing of the individual drug classes was conducted and reported in the supplementary material. NRI for missing outcomes of interest was also used in this subset analysis.

### Ethics

The protocol, amendments, and consent documentation were approved by local institutional review boards (IRBs). The study was conducted according to International Conference on Harmonization, Good Clinical Practice guidelines, and the Declaration of Helsinki. All patients were required to give informed consent for participation in the study. We confirm that the necessary central or local IRB and/or ethics committee approvals have been obtained for this multi-site, international study by United BioSource LLC (UBC). Approvals can be provided on request.

## RESULTS

Previous publications have detailed the comparisons in baseline demographics for the total number of patients enrolled in this study. For this post hoc analysis, patient profiles were comparable between drug classes with some exceptions. Overall, most patients included in this post hoc analysis were treated with anti-IL-17A/RA (*N* = 837), followed by anti-IL-23 (*N* = 657), anti-TNFα (*N* = 360), and anti-IL-12/23 (*N* = 127) (Table 1). The number of patients with sPGA score of 5 (very severe) was numerically higher in the anti-IL-17A/RA and anti-IL-23 cohorts compared to anti-IL-12/23 and anti-TNFα cohorts (4.5% and 4.8% vs. 1.6% and 1.7%, respectively). Also, in the anti-IL-17A/RA cohort, the percentage of patients with psoriatic arthritis was higher at 29.0% compared to anti-IL-23, anti-IL-12/23, and anti- TNFα cohorts (18.4%, 15.0%, and 21.7%, respectively). The anti-TNFα cohort had the highest percentage of patients receiving a prior conventional treatment compared to all other cohorts, whereas patients in the anti-IL-23 cohort had the highest percentage of patients receiving a prior biologic treatment. Regarding race, anti-IL-23 had the highest Asian population at 23.7% compared to anti-IL-17A/RA, anti-IL-12/23, and anti-TNFα cohorts (14.7%, 6.3%, and 2.5%, respectively). Similar trends were observed in the US on-label patient population (Supplementary Material, Table 1).

### Pairwise Comparison of the Anti-IL-17A/RA Drug Class vs. the Other Drug Classes

#### *Effectiveness Outcome*

For the unadjusted response rates, the percentage of patients who achieved primary, PASI100, and PASI90, outcomes were the highest for anti-IL-17A/RA at week 12, month 6, and month 12, except for anti-IL-23 at month 12, where similar response rates were observed (Fig. 1A–D). In the comparative, adjusted FMA analysis, patients treated with anti-IL-17A/RA had significantly higher odds of achieving the primary outcome compared to all other cohorts at week 12, anti-IL-12/23 and anti-TNFα at month 6, and anti-IL-12/23 at month 12 (Fig. 1A). Regarding PASI100 and PASI90, patients treated with anti-IL-17A/RA had significantly higher odds of achieving these outcomes at week 12 and month 6 compared to all other drug classes. At month 12, patients treated with anti-IL-17A/RA had significantly higher odds of achieving PASI100 compared to anti-IL-12/23 and anti-TNFα and

**Table 1** Baseline demographics

| | **Overall (*N* = 1981)** | **Anti-IL-17A/RA (*N* = 837)** | **Anti-IL-23 (*N* = 657)** | **Anti-IL-12/23 (*N* = 127)** | **Anti-TnFα (*N* = 360)** |
|---|---|---|---|---|---|
| Age, years | 45.3 (13.6) | 46.6 (13.7) | **44.3 (13.5)**** | 46.4 (14.5) | **44.0 (13.2)**** |
| Male, *n* (%) | 1143 (57.7) | 479 (57.2) | 397 (60.4) | 77 (60.6) | 190 (52.8) |
| Weight, kg | 85.0 (21.1) | 85.6 (20.8) | 84.6 (21.8) | 82.9 (17.1) | 85.2 (21.5) |
| BMI, kg/m$^2$ | 29.0 (6.7) | 29.3 (6.7) | 28.9 (6.8) | **28.0 (5.6)**** | 29.1 (6.8) |
| Race-White, *n* (%) | 1,441 (72.7) | 616 (73.6) | *421 (64.1)** | 99 (78.0) | *305 (84.7)** |
| Race-Asian, *n* (%) | 296 (14.9) | 123 (14.7%) | *156 (23.7)** | **8 (6.3)**** | *9 (2.5)** |
| Race-not reported, *n* (%) | 238 (12.0) | 95 (11.4) | 78 (11.9) | 19 (15.0) | 46 (12.8) |
| Median disease duration, years (Q1, Q3) | 14.0 (6.8, 23.8) | 14.3 (6.4, 23.7) | 14.1 (8.0, 23.9) | 12.1 (6.3, 23.7) | 13.4 (5.9, 23.8) |
| PASI total score | 14.5 (8.6) | 14.7 (8.5) | 14.9 (9.4) | 14.4 (7.9) | **13.5 (7.0)**** |
| % BSA | 21.3 (17.7) | 21.4 (17.6) | 21.0 (18.4) | 22.6 (17.7) | 21.4 (16.9) |
| sPGA, *n* (%) | | | | | |
| Moderate | 988 (50.7) | 424 (51.3) | 287 (44.6) | 68 (54.8) | 209 (59.0) |
| Severe | 610 (31.3) | 260 (31.5) | 221 (34.3) | 37 (29.8) | 92 (26.0) |
| Very severe | 76 (3.9) | 37 (4.5) | 31 (4.8) | 2 (1.6) | 6 (1.7) |
| DLQI[a] | 12.6 (7.8) | 12.9 (7.9) | **11.9 (7.7)**** | 12.3 (8.0) | 13.2 (7.6) |
| Any comorbidities reported, *n* (%) | 1157 (58.4) | 513 (61.4) | 369 (56.3) | 78 (61.4) | **197 (54.7)**** |
| Number of current comorbidities reported[b] | 1.5 (1.8) | 1.6 (1.8) | 1.5 (1.8) | 1.7 (2.1) | **1.3 (1.7)**** |
| Psoriatic arthritis, *n* (%)[c] | 461 (23.3) | 243 (29. 0) | *121 (18.4)** | *19 (15.0)** | **78 (21.7)**** |
| Nail psoriasis, *n* (%)[d] | 750 (37.9) | 324 (38. 7) | 253 (38.6) | 45 (35.7) | 128 (35.6) |
| Any previous conventional therapy, *n* (%) | 1565 (79.0) | 627 (75.0) | 507 (77.2) | **106 (83.5)**** | *325 (90.3)** |
| Any previous biologic therapy, *n* (%)[e] | 706 (35.7) | 314 (37.6) | *319 (48.6)** | **35 (27.6)**** | *38 (10.6)** |

All results are expressed as mean (standard deviation) of all available data for that measure, unless otherwise indicated

*BMI* body mass index, *BSA* body surface area, *DLQI* Dermatology Life Quality Index, *IL* interleukin, *n* number of patients

**Table 1** continued

who achieved the outcome, *N* total number of patients in treatment group, *PASI* Psoriasis Area and Severity Index, *PsA* psoriatic arthritis, *Q1* quartile 1, *Q3* quartile 3, *sPGA* static Physician Global Assessment, *TNF* tumor necrosis factor

**$P$ value < 0.05 vs. anti-IL-17A/RA (given in bold)

*$P$ value < 0.001 vs. anti-IL-17A/RA (given in italics)

[a]DLQI was measured on a 0–30 scale

[b]Comorbidities were captured based on a predefined list

[c]PsA diagnosis was recorded by the dermatologists based on the medical history and/or information provided by the patient

[d]Recorded as a simple yes/no question (investigator assessed)

[e]Information about prior biologic use missing in 1 patient

significantly higher odds of achieving PASI90 compared to anti-IL-12/23.

### *Quality of Life outcome*

Across the drug classes, the unadjusted response rates for DLQI (0,1) ranged from 22.8–39.3% at week 12, 30.5–38.4% at month 6, and 31.8–33.0% at month 12 (Fig. 1D). Anti-IL-17A/RA had the highest unadjusted response rates at week 12 (39.3%) and month 6 (38.4%), with anti-IL-23 displaying the highest unadjusted response rates at month 12 (33.0%). For the adjusted analyses, anti-IL-17A/RA showed statistically significantly higher odds of achieving DLQI (0,1) at week 12 compared to all other drug classes, and statistically significantly higher odds of achieving this outcome compared to anti-IL-23 and anti-TNFα at month 6, with no statistically significant differences being observed at month 12 between drug classes.

### *Durability of Effectiveness Outcome*

For the first durability of effectiveness outcome (patients who met the primary outcome at week 12 and who subsequently at months 6 and 12 achieved an improvement of at least PASI75 and/or 2 or more points in sPGA score from baseline [13]), anti-IL-17A/RA patients had the highest response rate (52.6%), and, for the FMA adjusted analysis, patients had 1.4–2.6 times higher odds of achieving the primary durability outcome compared to patients treated with any other drug class (Fig. 2A). Regarding the PASI100 and PASI90 durability of effectiveness outcomes, anti-IL-17A/RA patients had the highest response rate of 18.3% and 35.2%, respectively (Fig. 2B and C). Furthermore, anti-IL-17A/RA had significantly higher odds of achieving PASI100 and PASI90 durability of effectiveness outcomes compared to patients treated with any other drug class, with OR ranging from 1.3 to 3.0.

## DISCUSSION

The analysis of PSoHO data presented extends on previously published week 12 [12] and month 12 [13] data and gives insights into patient outcomes and response dynamics of different drug classes. At week 12, anti-IL-17A/RA showed a statistically significant higher odds of achieving the primary outcome, PASI90 and/or sPGA score of 0 or 1, compared to all other drug classes. This aligns with other studies that found that biologics targeting the IL-17 cytokine pathway are associated with a more rapid onset of treatment response relative to other biologics [18–21]. Furthermore, anti-IL-17A/RA showed a numerically higher response rate of achieving the primary outcome at month 6 and month 12, except for anti-IL-23 at month 12, compared to other drug classes. Similar trends were observed for the US on-label patient population (Supplementary Material, Fig. 1).

A recent study has shown that drug classes inhibiting IL-17 or IL-23 were associated with the most favorable efficacy outcomes compared with biologics blocking TNFa or IL-12/23

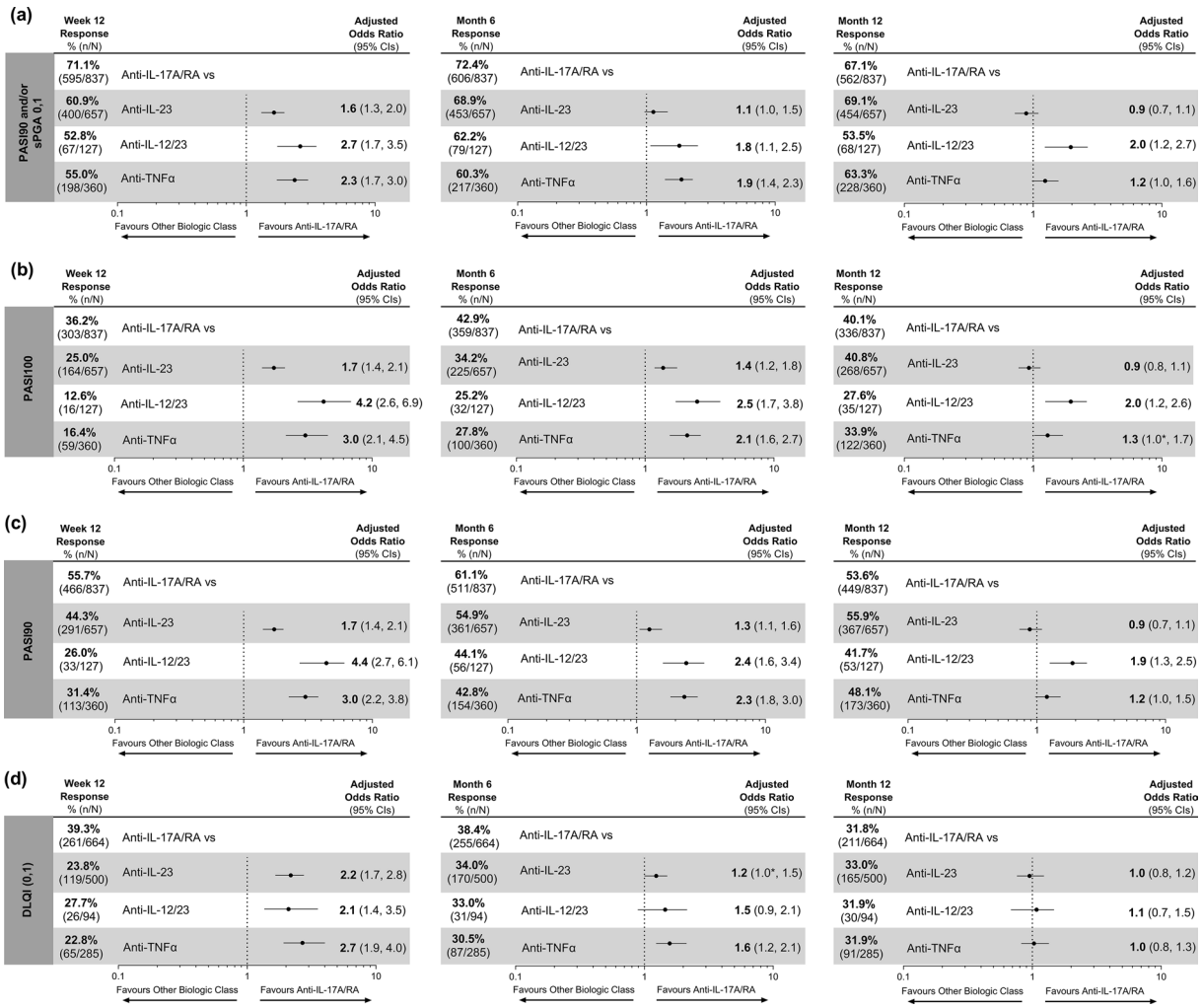


**Fig. 1** Unadjusted response rates and comparative adjusted odds ratios for primary and secondary outcomes for anti-IL-17A/RA versus other drug classes. **A** Primary outcome of PASI90 and/or sPGA score of 0 or 1 at week 12, month 6, and month 12. **B** PASI100 at week 12, month 6, and month 12. **C** PASI90 at week 12, month 6, and month 12. **D** DLQI score of 0 or 1 at week 12, month 6, and month 12. DLQI outcome only included patients with an available DLQI score of 2 or greater at baseline. Results are statistically significant if 95% CIs of the odds ratios do not cross 1. For instances that lower CI shows 1.0, * denotes that lower CI is greater than 1. If 1.0 is shown, then it is actually below 1 and not significant. *CI* confidence interval, *DLQI* Dermatology Life Quality Index, *IL* interleukin, *n* number of patients who achieved the outcome, *N* total number of patients in treatment group, *PASI* Psoriasis Area and Severity Index, *PASI90* 90% improvement in the PASI score, *PASI100* 100% improvement in the PASI score, *sPGA* static Physician Global Assessment, *TNF* tumor necrosis factor

[22, 23], and PSoHO adds to these studies by providing outcomes up to 12 months in the real-world setting. In this post hoc analysis, for PASI100 and PASI90 outcomes at week 12, anti-IL-17A/RA showed statistically significant higher odds of reaching this outcome compared to all other drug classes. This is in line with previously published network meta-analysis of randomized controlled trials that IL-17 inhibitors show a higher efficacy profile compared to other drugs in terms of PASI90 and PASI100 [22, 24]. Additionally, for PASI100 and PASI90 outcomes, the highest unadjusted response rates were achieved with anti-IL-17A/RA at week

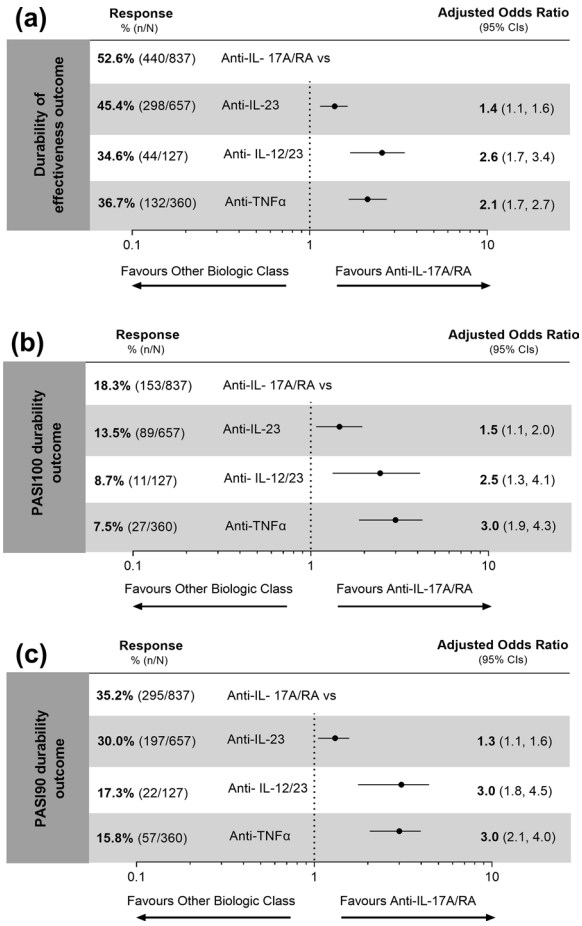


**Fig. 2** Unadjusted response rates and comparative adjusted odds ratios for durability of effectiveness outcomes for anti-IL-17A/RA versus other drug classes. Outcomes include **A** durability of effectiveness outcome, whereby patients achieve at least PASI90 and/or sPGA score of 0 or 1 at week 12 and subsequently achieve either or both of the following outcomes at months 6 and 12: at least PASI75 or achieving an improvement in sPGA of 2 or more points from baseline. **B** PASI100 durability outcome, whereby patients achieve a PASI100 score at week 12 and subsequently at both months 6 and 12. **C** PASI90 durability outcome, whereby patients achieve a PASI90 score at week 12 and subsequently at both months 6 and 12. Results are statistically significant if 95% CIs of the odds ratios do not cross 1. *CI* confidence interval, *IL* interleukin, *n* number of patients who achieved the outcome, *N* total number of patients in treatment group, *PASI* Psoriasis Area and Severity Index, *PASI75* 75% improvement in the PASI score, *PASI90* 90% improvement in the PASI score, *PASI100* 100% improvement in the PASI score, *sPGA* Static Physician Global Assessment, *TNF* tumor necrosis factor

12 and month 6. At week 12, anti-IL-17A/RA unadjusted response rates were followed by anti-IL-23, TNFα, and anti-IL-12/23, which is in line with previously reported findings [25]. At month 12, anti-IL-23 had a 0.7%-point higher unadjusted PASI100 response rate (40.8% vs. 40.1%) and a 2.3%-point higher unadjusted PASI90 response rate (55.9% vs. 53.6%) compared to anti-IL-17A/RA. The response dynamics may reflect the different mechanism of action of the various drug classes [26], whereby anti-IL-23 have a slower response rate compared to anti-IL-17A/RA at week 12. However, both drug classes display comparable results at month 12. This is evidenced by the finding that anti-IL-17A/RA showed the highest odds of achieving PASI90 and PASI100, compared to all other drug classes at week 12. By month 12, anti-IL-17A/RA and anti-IL-23 provided the greatest unadjusted responses with no significant differences in adjusted OR between these 2 drug classes. These results support previously published data that biologics that target IL-17 cytokines are associated with a rapid onset of response, and patients who were early responders were more likely to achieve a stable response of PASI90 or PASI100 [27]. In total, these results emphasize the importance of the speed of clinical improvement when selecting a biologic agent, an often-overlooked aspect in clinical studies but one of the most important features for patients [13, 20, 28].

Studies have shown that IL-17A and IL-17RA biologics result in higher DLQI (0,1) responses at week 12 [29] and comparable response rates to other drugs by month 12 [13]. The results in this post hoc analysis are in accordance with these published findings, as the unadjusted response rates for DLQI (0,1) were higher for the anti-IL-17A/RA-treated patients at week 12 and month 6 compared to all other drug classes, with statistically higher odds of reaching these responses rates at week 12. At month 12, response rates were similar among the different drug classes. Between week 12 and month 12, the difference in response rates lowered between the drug classes from 16.5 to 1.2%, and, by month 12, there was no significant difference in adjusted OR between the drug classes, potentially because of differing mechanisms of action between

treatment drug classes. Anti-IL-17A/RA displays a fast onset of action, which results in higher DLQI (0,1) response at week 12; other drug classes that display slower onset of action and lower DLQI (0,1) response at week 12 only have similar impact on the patient's quality of life compared to anti-IL-17A/RA-treated patients by month 12. Similar results were observed for the US on-label population (Supplementary Material, Fig. 2).

Overall, when investigating biologics for PsO, studies usually provide evidence based on individual drugs rather than drug class [23]. While a published retrospective, multi-country, real-world study provides insights into the drug survival of IL-12/23, IL-17, and IL-23 inhibitors [30], PSoHO adds to this by providing additional real-world drug class effectiveness data and durability of effectiveness up to 12 months. When looking at the achievement of response at week 12 and maintaining responses at months 6 and 12, anti-IL-17A/RA had a 1.3–3.0 times higher odds of demonstrating response durability versus all other drug classes. Durability is crucial for the continuous effective treatment of PsO. Of note, by investigating effectiveness at 3 time points over the course of 12 months, PSoHO gives better insight into the varying response dynamics of different drug classes. Overall, better understanding of the onset of treatment and continued effectiveness in a real-world setting can help to inform treatment decisions that dermatologists face when comparing numerous approved biologics.

This post hoc analysis has some limitations. Comparisons of drug class effectiveness were completed relative to anti-IL-17A/RA biologics only, and did not include non-biologic drugs. Additionally, by comparing at drug class level, there is a lack of granularity and the heterogeneous effectiveness of individual biologics within drug classes is not taken into account [31, 32]. However, by focusing on drug classes, data are pooled from multiple individual biologics, leading to more statistically robust results. Reporting on both individual biologics and drug classes has its merits, and a balanced approach that considers both individual biologics as well as drug classes can provide a better understanding of the effectiveness of psoriasis treatments based on the underlying pharmacodynamic properties. Therefore, the results presented here should be considered with previously published 12-month outcomes at an individual biologic level [13], which together bridge the gap between clinical studies and various guideline recommendations. Taken together, the published 12-month outcomes [13] and this study support clinicians in choosing the correct biological treatment by providing information on biologic drug classes and individual biologics in terms of commonalities and differences.

Compared to randomized controlled trials, observational studies have inherent limitations, such as selection bias and confounding by indication, which partly explain the disparities in the observed samples sizes. With respect to the analyses, the highest proportion of patients were prescribed anti-IL-17A/RA class, translating to higher statistical precision, whereas the other biological drug classes had fewer patients. This disparity in sample sizes, however, is accounted for within the confidence intervals, reflecting the uncertainty around the observed estimates. Additionally, both measured and unmeasured confounding factors, from both the investigator and patient perspectives, also poses challenges for the data analysis. However, PSoHO's unique application of the FMA machine-learning approach adjusts for confounding factors relating to patient disease characteristics and demographics. Additionally, the robustness of the analysis is confirmed by the E-value analysis, showing that substantial confounding that exceeds the effect of established confounders, such as current topical treatment or current non-biologic treatment, would be required to impact the observed responses through unmeasured confounders. Whether these limitations challenge the conclusions of this study remains to be seen in larger future studies.

## CONCLUSION

Building on previously published PSoHO data, these latest results directly compare the

effectiveness and durability of different drug classes through 12 months for patients with moderate-to-severe plaque PsO in the real-world setting. The results highlight that speed of response with different drug classes may be due to different mechanism of actions. Overall, anti-IL-17A/RA had the highest effectiveness of achieving early response to treatment and maintaining that response through 12 months compared to other drug classes.

***Medical Writing/Editorial Assistance.*** In addition to participating as author, Caroline A. Murphy provided medical writing assistance with the preparation of this manuscript, funded by Eli Lilly and Company.

***Author Contributions.*** Saakshi Khattri: Interpretation of data, critical revision of the work for important intellectual content. Álvaro González-Cantero: Analysis of data, drafting of the manuscript, critical revision of the work for important intellectual content. Burhan Engin: Acquisition of data, interpretation of data, critical revision of the work for important intellectual content. Sunil Dogra: Interpretation of data, critical revision of the work for important intellectual content. Caroline A. Murphy: interpretation of data for the work, drafting. Christopher Schuster: interpretation of data, drafting the manuscript, critical revision of the work for important intellectual content. Naoto Tsujimoto: analysis of data, interpretation of data, critical revision of the work for important intellectual content. Georgia Martimianaki: Analysis of data, critical revision of the work for important intellectual content. Anastasia Lampropoulou: interpretation of data, critical revision of the work for important intellectual content. Aya Alsharafi: Analysis of data, interpretation of data, drafting and critical revision of the work for important intellectual content. Bruce Konicek: interpretation of data, critical revision of the work for important intellectual content. Felix Lauffer: interpretation of data, critical revision of the work for important intellectual content.

***Funding.*** This study was funded by Eli Lilly and Company. The funder of the study had a role in study design, data analysis, data collection, data interpretation, and writing of the report. All publishing fees including the Rapid Service Fee and Open Access Fee were sponsored by Eli Lilly and Company.

***Data Availability.*** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. Lilly provides access to all individual participant data collected during the study, after anonymization. Data are available to request after primary publication acceptance. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

## *Declarations*

***Conflict of Interest.*** Saakshi Khattri is a speaker for AbbVie, Janssen, Lilly, and UCB; serves as an advisory board member/consultant for AbbVie, Janssen, Lilly, Novartis, and UCB; and has received research grants from AbbVie, BMS, LEO, Novartis, and Pfizer; Álvaro González-Cantero has served as a consultant for and received speaker fees from AbbVie, Janssen, Novartis, Almirall, Celgene, UCB, L'Oreal, MSD and Leo Pharma; Burhan Engin and Sunil Dogra has no conflict of interest to declare; Caroline A. Murphy, Christopher Schuster, Naoto Tsujimoto, Georgia Martimianaki, Anastasia Lampropoulou, Aya Alsharafi and Bruce Konicek are employees and shareholders of Eli Lilly and Company; Felix Lauffer has received speaker or consultant fees from Abbvie, Novartis Pharma, LEO Pharma, Lilly, Roche, Sanofi, Almirall, Janssen-Cilag Pharma Amgen, UCB Pharma,

Boehringer-Ingelheim, Bristol-Myers-Squibb, and Union Therapeutics.

***Ethical Approval.*** The protocol, amendments, and consent documentation were approved by local institutional review boards (IRBs). The study was registered at the European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCEPP24207) and was conducted according to International Conference on Harmonization, Good Clinical Practice guidelines, and the Declaration of Helsinki. All patients were required to give informed consent for participation in the study. We confirm that the necessary central or local IRB and/or ethics committee approvals have been obtained for this multi-site, international study by United BioSource LLC (UBC). Approvals can be provided on request.



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