

Effectiveness of adalimumab and secukinumab with and without concomitant csDMARD in psoriatic arthritis patients: retrospective cohort study

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Abstract

Background

To compare the effectiveness of biologic disease-modifying antirheumatic drugs (bDMARDs) with and without concomitant conventional synthetic DMARDs (csDMARDs) in terms of bDMARD drug retention in psoriatic arthritis (PsA) patients.

Methods

PsA patients starting first-line bDMARD adalimumab and/or second-line bDMARD secukinumab between November 2019 and March 2025 were included and categorized as bDMARD monotherapy or as combination therapy (bDMARD with concomitant csDMARD). Patients ineligible for combination therapy (csDMARD contraindications or side effects) were excluded. bDMARD discontinuation due to side effects or ineffectiveness was counted as an event. Individual patients could contribute data to both adalimumab and secukinumab analyses. Primary outcome was bDMARD drug retention, analyzed using Kaplan-Meier curves and multivariable Cox regression adjusted for age and sex.

Results

635 PsA patients were included: 183 adalimumab monotherapy and 318 combination therapy; 136 secukinumab monotherapy and 125 combination therapy. The csDMARDs in the combination therapy were mostly methotrexate (65–67%) or leflunomide (21–30%). Adalimumab combination therapy showed significantly lower discontinuation risk in unadjusted (median retention 11.0 vs 15.0 months, hazard risk 0.71, $p = 0.012$) and adjusted analyses (adjusted hazard risk 0.67, $p = 0.003$) compared to adalimumab monotherapy. In secukinumab, no significant difference was observed for monotherapy versus combination therapy (median retention 10.6 vs 7.3 months, hazard risk 1.11, $p = 0.50$ and adjusted hazard risk 1.14, $p = 0.42$). The effect of csDMARD use was significantly greater in adalimumab compared to secukinumab (interaction: $p = 0.028$).

Conclusion

Concomitant csDMARD use significantly prolonged drug retention for adalimumab but not for secukinumab, suggesting csDMARDs should be continued when starting adalimumab but may be discontinued when starting secukinumab.

Background

Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by psoriasis and musculoskeletal manifestations including arthritis, dactylitis, enthesitis and sacroiliitis/spondylitis (1).

As PsA is associated with irreversible joint damage and decreased quality of life, effective treatment strategies targeting remission are essential (2).

International European Alliance of Associations for Rheumatology (EULAR) and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines recommend conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate (MTX), sulfasalazine and leflunomide (LEF) as first-line therapy after non-steroidal anti-inflammatory drugs (NSAIDs) and local glucocorticoids (3, 4). While supported by favourable safety profiles, low cost, and accessibility, evidence for their efficacy in PsA remains limited, particularly for arthritis (3, 5–14).

Biologic DMARDs (bDMARDs) including tumor necrosis factor inhibitors (TNFi) and interleukin-17 inhibitors (IL-17i) demonstrate superior efficacy compared to csDMARDs (15–17). However, whether csDMARDs should be continued or combined when initiating these bDMARDs remains debated. The American College of Rheumatology (ACR) conditionally recommends switching to bDMARD monotherapy after csDMARD failure, thus discontinuing the csDMARD (18). In contrast, EULAR advises to continue the csDMARD, particularly if the csDMARD is well tolerated and in case of starting a TNFi, noting a lack of data on comedication efficacy for other classes of bDMARDs (3). The rationale for combining csDMARDs with bDMARDs potentially includes the residual efficacy of csDMARDs, the synergistic therapeutic effect, and reduction of anti-drug antibody (ADA) formation.

In rheumatoid arthritis (RA), randomized controlled trials have demonstrated that concomitant MTX enhances early and late TNFi efficacy, whereas comparable evidence for LEF is lacking. Observational studies further suggest that concomitant MTX enhances long-term treatment persistence (19–22). In PsA, controlled cohort study data suggest combining bDMARDs with csDMARDs extends TNFi persistence, though not for IL-17i or IL-23i (23–26). Systematic reviews also report enhanced skin responses with combination therapy but limited evidence for joint-specific benefits (6, 27). Regarding joint disease activity, results are inconclusive. Some analyses suggest improved clinical response with combination therapy (6, 27, 28), whereas randomized clinical trial-based network meta-analyses report no significant difference in arthritis outcomes (27, 29, 30). Methodological heterogeneity limits interpretation, and the most consistent finding is improved drug retention rather than superior remission rates (24, 27). GRAPPA recommendations acknowledge that further study is needed (31).

Since csDMARDs require laboratory monitoring, lead to patient burden and carry adverse effect risks (32), clarifying their added value when initiating adalimumab and secukinumab, is clinically relevant. This study aims to evaluate whether concomitant csDMARD use affects bDMARD drug retention in PsA patients treated with bDMARDs, and whether this effect differs between adalimumab and secukinumab.

Methods

Study design

A retrospective cohort study was conducted at the Sint Maartenskliniek Rheumatology outpatient clinic in the Netherlands. Data from November 2019 until September 2025 were extracted from the standardized Integrated Rheumatology Information System (IRIS), in which clinical data of all rheumatology patients who visited the Sint Maartenskliniek are stored, to minimize information bias. Extracted data included demographic and clinical characteristics: age, sex, body mass index (BMI), smoking, disease duration, anti-citrullinated protein (anti-CCP) and rheumatoid factor (RF); disease activity parameters: Disease Activity Score 28 with CRP (DAS28-CRP), C-reactive protein (CRP), tender joint score (TJC), swollen joint score (SJC) and visual analog scale for patient global assessment (VAS) (33); and medication history: cs/b/tsDMARD usage (name, class, start and stop dates and reason for treatment discontinuation, including side effects, inefficacy, remission, injection reaction, pregnancy, deceased and other reasons).

Study population

The study size was determined by the availability of data within the IRIS registry during the specified study period, thus no formal a priori sample size calculation was performed, as the cohort size was fixed by the IRIS registry population. All patients with a clinical diagnosis of PsA who started either adalimumab and/or secukinumab between November 2019 until March 2025 (to allow for a minimum of 6 months follow up). Patients with contraindications to csDMARD usage (including significant adverse effects, pregnancy, hepatic or renal impairment or primarily axial manifestations that dictated the prescription of bDMARD) were excluded from the study to minimize confounding by indication. Data was extracted from routine care, in a clinical setting where the local treatment protocol stated that, unless (contra-)indications dictated otherwise, adalimumab was to be prescribed as first-line bDMARD and secukinumab was to be prescribed as second-line bDMARD.

Eligible patients were subsequently assigned into a bDMARD “monotherapy group” or a bDMARD plus csDMARD “combination therapy group”. Patients were assigned to the monotherapy group when no concomitant csDMARD use overlapped with the start date of the bDMARD, or when overlap was limited to a maximum of one month. Patients were assigned to the combination therapy group when there was at least one month of concomitant csDMARD use, counted from the bDMARD start date or if csDMARD use overlapped with the entire bDMARD treatment period. Baseline was defined as the date of initiation of adalimumab and/or secukinumab. Since both adalimumab and secukinumab were included in this study and treatment strategies could change over time, individual patients who received both biologics could contribute data to both the adalimumab and secukinumab treatment groups.

Outcome measures

The primary outcome was the bDMARD drug retention rate. Secondary outcomes included the bDMARD drug retention at 6, 12 and 24 months. Drug retention was calculated from the start date to the stop date or censoring date of the bDMARD. bDMARD treatment discontinuation because of side effects or inefficacy were considered events. Patients who discontinued the bDMARD for other reasons (e.g.,

remission, patient preference) were censored at the date of discontinuation. Patients who remained on treatment at the date of data extraction or were lost to follow-up were censored at their last documented outpatient visit.

Statistical analysis

Statistical analyses were performed using R (version 4.5.1). Baseline characteristics were summarized using descriptive statistics and compared between adalimumab monotherapy and combination therapy and secukinumab monotherapy and combination therapy. Continuous variables were reported as median with interquartile range (IQR) for non-normally distributed data and categorical variables were reported as frequencies (*n*) and percentages. Between-group comparisons were performed using Mann-Whitney U test for non-normally distributed continuous variables, and Chi-square test or Fisher's exact test for categorical variables.

Drug retention was assessed using Kaplan–Meier curves. Hazard ratios (HRs) for the risk of bDMARD discontinuation were estimated using multivariable Cox regression models, adjusted for potential confounders, including age (based on between-group differences in our data) and sex (based on association with drug retention reported in literature)(34). The following comparisons of drug retention were performed: (1) adalimumab monotherapy versus adalimumab in combination with csDMARDs, (2) secukinumab monotherapy versus secukinumab in combination with csDMARDs, and (3) the interaction between csDMARD use and bDMARD type (adalimumab versus secukinumab). Since drug retention dates, age, and sex are mandatory fields in the IRIS registry, missing data in the primary analysis covariates were not applicable.

A sensitivity analysis was per-protocol conducted based on concomitant csDMARD use. For the per-protocol analysis, patients in the combination therapy group were censored when all concomitant csDMARD were discontinued and patients in the monotherapy group were censored at concomitant csDMARD initiation. Exploratory analysis was conducted based on csDMARD type.

Results

Patient characteristics

In total 635 PsA patients were included, of whom 183 and 318 were assigned to the adalimumab monotherapy and combination therapy groups, respectively, and 136 and 125 to the secukinumab monotherapy and combination therapy groups, respectively. Baseline characteristics are presented in Tables 1 and 2. For both adalimumab and secukinumab, patients receiving combination therapy were slightly older and had greater prior csDMARD exposure. In the secukinumab cohort, the combination therapy group also had a longer disease duration at treatment initiation. No other meaningful baseline differences were observed. Reasons for treatment discontinuation and censoring are presented in Supplementary Table S1.

Table 1
Baseline characteristics by adalimumab monotherapy and combination therapy

Variable	Adalimumab monotherapy N = 183	Adalimumab combination therapy N = 318	p-value¹
Age (years), median (Q1, Q3)	48 (34, 58)	50 (39, 59)	0.05
Sex (female), N (%)	94 (51%)	166 (52%)	0.86
BMI, median (Q1, Q3) ^a	26.8 (24.2, 30.0)	26.7 (23.9, 30.2)	> 0.99
Smoking status, N (%)			0.32
Never	59 (54%)	85 (45%)	
Stopped	31 (28%)	59 (31%)	
Currently	20 (18%)	45 (24%)	
Unknown	73	129	
Disease duration (years), median (Q1, Q3)	1.0 (0.0, 3.0)	1.0 (0.0, 4.0)	0.18
Anti-citrullinated protein, N (%)			> 0.99
Negative	120 (99%)	215 (99%)	
Positive	1 (0.8%)	3 (1.4%)	
Unknown	62	100	
Rheumatoid factor, N (%)			0.23
Negative	112 (96%)	191 (92%)	
Positive	5 (4.3%)	16 (7.7%)	
Unknown	66	111	
DAS28-CRP, median (Q1, Q3) ^b	3.2 (2.3, 3.9)	3.0 (2.4, 3.7)	0.65
TJC, median (Q1, Q3) ^c	2 (0, 4)	1 (0, 3)	0.40

¹Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's Exact Test for Count Data. Number available: a = 88 for monotherapy and 151 for combination therapy, b = 65 for monotherapy and 116 for combination therapy, c = 68 for monotherapy and 112 for combination therapy, d = 66 for monotherapy and 120 for combination therapy, e = 65 for monotherapy and 115 for combination therapy. N, number; Q, quartile; BMI, body mass index; DAS28-CRP, Disease Activity Score 28; TJC, tender joint score; SJC, swollen joint score; CRP, C-reactive protein; csDMARD, conventional Disease-Modifying Anti Rheumatic Drugs; b/tsDMARD, biological or targeted-synthetic Disease-Modifying Anti Rheumatic Drugs.

Variable	Adalimumab monotherapy N = 183	Adalimumab combination therapy N = 318	p-value¹
SJC, median (Q1, Q3) ^d	1 (0, 3)	1 (0, 2)	0.62
CRP, median (Q1, Q3) ^e	5 (2, 10)	4 (2, 10)	0.44
Concomitant csDMARD, N (%)			
Leflunomide		66 (21%)	
Leflunomide + methotrexate		33 (10%)	
Methotrexate		212 (67%)	
Methotrexate + sulfasalazine		7 (2.2%)	
Number of previously used b/tsDMARDs, N (%)	177 (97%)	312 (98%)	0.40
0	6 (3.3%)	6 (1.9%)	
1			
Number of previously and/or currently csDMARDs, N (%)	20 (11%)	2 (0.6%)	< 0.001
0	93 (51%)	166 (52%)	
1	64 (35%)	135 (42%)	
2	6 (3.3%)	15 (4.7%)	
3 or more			
¹ Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's Exact Test for Count Data. Number available: a = 88 for monotherapy and 151 for combination therapy, b = 65 for monotherapy and 116 for combination therapy, c = 68 for monotherapy and 112 for combination therapy, d = 66 for monotherapy and 120 for combination therapy, e = 65 for monotherapy and 115 for combination therapy. N, number; Q, quartile; BMI, body mass index; DAS28-CRP, Disease Activity Score 28; TJC, tender joint score; SJC, swollen joint score; CRP, C-reactive protein; csDMARD, conventional Disease-Modifying Anti Rheumatic Drugs; b/tsDMARD, biological or targeted-synthetic Disease-Modifying Anti Rheumatic Drugs.			

Table 2
Baseline characteristics by secukinumab monotherapy and combination therapy

Variable	Secukinumab monotherapy N = 136	Secukinumab combination therapy N = 125	p-value¹
Age (years), median (Q1, Q3)	52 (37, 60)	54 (47, 62)	0.01
Sex (female), N (%)	78 (57%)	74 (59%)	0.76
BMI, median (Q1, Q3) ^a	26.9 (23.8, 30.8)	27.7 (25.1, 31.2)	0.16
Smoking status, N (%)			0.18
Never	39 (56%)	33 (42%)	
Stopped	16 (23%)	28 (36%)	
Currently	15 (21%)	17 (22%)	
Unknown	66	47	
Disease duration (years), median (Q1, Q3)	3.0 (1.0, 9.0)	5.0 (2.0, 11.0)	0.01
Anti-citrullinated protein, N (%)			0.48
Negative	94 (100%)	86 (99%)	
Positive	0 (0%)	1 (1.1%)	
Unknown	42	38	
Rheumatoid factor, N (%)			0.31
Negative	91 (97%)	79 (93%)	
Positive	3 (3.2%)	6 (7.1%)	
Unknown	42	40	
DAS28-CRP, median (Q1, Q3) ^b	3.1 (2.3, 3.8)	3.3 (2.4, 4.3)	0.13
TJC, median (Q1, Q3) ^c	1 (0, 4)	3 (0, 6)	0.13

¹Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's Exact Test for Count Data. Number available: a = 85 for monotherapy and 80 for combination therapy, b = 45 for monotherapy and 50 for combination therapy, c = 47 for monotherapy and 53 for combination therapy, d = 47 for monotherapy and 53 for combination therapy, e = 45 for monotherapy and 50 for combination therapy. N, number; Q, quartile; BMI, body mass index; DAS28-CRP, Disease Activity Score 28; TJC, tender joint score; SJC, swollen joint score; CRP, C-reactive protein; csDMARD, conventional Disease-Modifying Anti Rheumatic Drugs; b/tsDMARD, biological or targeted-synthetic Disease-Modifying Anti Rheumatic Drugs.

Variable	Secukinumab monotherapy N = 136	Secukinumab combination therapy N = 125	p-value ¹
SJC, median (Q1, Q3) ^d	1 (0, 3)	1 (0, 3)	0.80
CRP, median (Q1, Q3) ^e	3 (1, 6)	4 (1.25, 9.75)	0.23
Concomitant csDMARD, N (%)			
Leflunomide		37 (30%)	
Leflunomide + methotrexate		2 (1.6%)	
Leflunomide + sulfasalazine		1 (0.8%)	
Methotrexate		81 (65%)	
Methotrexate + sulfasalazine		4 (3.2%)	
Number of previously used b/tsDMARDs, N (%)	12 (8.8%)	5 (4.0%)	0.20
0	114 (84%)	114 (91%)	
1	10 (7.3%)	6 (4.8%)	
2 or more			
Number of previously and/or currently csDMARDs, N (%)	13 (96%)	0 (0%)	0.001
0	58 (43%)	43 (34%)	
1	50 (37%)	60 (48%)	
2	15 (11%)	22 (18%)	
3 or more			
Retention of previous b/tsDMARD (months), median (Q1, Q3)	9 (5, 29)	12 (5, 44)	0.23
¹ Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's Exact Test for Count Data. Number available: a = 85 for monotherapy and 80 for combination therapy, b = 45 for monotherapy and 50 for combination therapy, c = 47 for monotherapy and 53 for combination therapy, d = 47 for monotherapy and 53 for combination therapy, e = 45 for monotherapy and 50 for combination therapy. N, number; Q, quartile; BMI, body mass index; DAS28-CRP, Disease Activity Score 28; TJC, tender joint score; SJC, swollen joint score; CRP, C-reactive protein; csDMARD, conventional Disease-Modifying Anti Rheumatic Drugs; b/tsDMARD, biological or targeted-synthetic Disease-Modifying Anti Rheumatic Drugs.			

Retention time

Drug retention times are presented in Fig. 1a and 1b. The median drug retention for the adalimumab monotherapy group was 11.0 months (IQR 5.3–26.3), compared with 15.0 months (IQR 6.6–33.1) for the adalimumab combination therapy group. For secukinumab, the median drug retentions were 10.6 months (IQR 4.7–21.2) for the monotherapy group and 7.3 months (IQR 4.2–24.1) for the combination therapy group.

Patients receiving adalimumab combination therapy had a significantly lower risk of treatment discontinuation compared with those receiving adalimumab monotherapy in the unadjusted analysis (HR = 0.71, 95% CI 0.54–0.93, $p = 0.012$) and after adjustment for age and sex (adjusted HR = 0.67, 95% CI 0.51–0.87, $p = 0.003$). For patients receiving secukinumab there was no significant difference in drug retention between monotherapy and combination therapy in the unadjusted analysis (HR = 1.11, 95% CI 0.82–1.51, $p = 0.50$) and after adjustment for age and sex (HR = 1.14, 95% CI 0.83–1.56, $p = 0.42$). The added value of csDMARD use was significantly greater for adalimumab compared to secukinumab users, as demonstrated by a significant interaction between bDMARD type and csDMARD use (adjusted interaction HR = 1.59, 95% CI 1.05–2.39, $p = 0.028$).

The per-protocol analysis censored patients in the combination therapy group at the earliest occurrence of all concomitant csDMARD discontinuation and patients in the monotherapy group censored at the earliest occurrence of either concomitant csDMARD initiation. In this analysis, adalimumab combination therapy was again associated with a significantly lower risk of treatment discontinuation compared with monotherapy (adjusted HR = 0.62, 95% CI: 0.46–0.84, $p = 0.002$; Supplementary Figure S1a). For secukinumab, combination therapy showed a non-significant increase in hazard compared with monotherapy (adjusted HR = 1.22, 95% CI: 0.87–1.72, $p = 0.25$; Supplementary Figure S1b). Exploratory analysis by csDMARD type showed that for adalimumab, both MTX-based and LEF-based combination therapy appeared to be associated with longer drug retention compared to monotherapy (Supplementary Figure S2a). For secukinumab, drug retention curves for MTX-based combination therapy, LEF-based combination therapy, and monotherapy showed no clear separation (Supplementary Figure S2b).

Discussion

In this large retrospective study, we aimed to compare the effectiveness of adalimumab and secukinumab therapy with and without concomitant csDMARD use in patients with PsA in terms of drug retention. For adalimumab, combination therapy was consistently associated with significantly prolonged drug retention compared with monotherapy, both in (un)adjusted analyses and in the per-protocol sensitivity analysis. In contrast, no significant effect of concomitant csDMARDs was observed for secukinumab, with drug retention remaining comparable between monotherapy and combination therapy. The significant interaction between bDMARD type and csDMARD use underscores that the value of combination therapy differs between adalimumab and secukinumab.

The prolonged drug retention observed with adalimumab combination therapy aligns with other observational studies demonstrating longer TNFi retention when combined with methotrexate in PsA.

Several large European registry analyses, including the Norwegian NOR-DMARD study and the EuroSpA collaboration, have consistently reported superior TNFi drug retention with concomitant methotrexate use (23, 28, 35). Our findings are consistent with these reports and with recent systematic reviews showing improved TNFi persistence with methotrexate co-medication (24). However, our findings contrast with some recent data of the RABBIT-SpA registry. This registry reported no difference in drug retention between b/tsDMARD monotherapy and combination therapy with methotrexate (29). This discrepancy may reflect differences in study populations, as the RABBIT-SpA cohort included axial spondyloarthritis with multiple bDMARD classes analyzed together.

The absence of benefit for secukinumab combination therapy aligns with prior pharmacological and clinical evidence suggesting that IL-17i do not require csDMARD co-administration to maintain efficacy (36). The reason that csDMARDs lack a benefit to secukinumab drug retention rates is not clear. What is known is that secukinumab has demonstrated exceptionally low immunogenicity in clinical studies, with ADA rates below 1% over five years of follow-up, and no evidence that the formation of these ADA affects the drug's pharmacokinetics, efficacy, or safety profile (37, 38). This low immunogenic potential reduces part of the theoretical rationale for concomitant immunosuppressive co-medication to preserve drug efficacy. Notably, this low immunogenic potential may reflect not only the mechanism of action but also the structural properties of the molecule itself. Another potential explanation is the superior effect of secukinumab to clear concomitant psoriasis, possibly indirectly reducing the margin by which adding csDMARDs can provide supplemental benefit to overall clinical efficacy when treating PsA. Overall, our observations are consistent with systematic reviews and network meta-analyses that have consistently reported no added value of csDMARDs with IL-17i, with comparable effectiveness and safety profiles between monotherapy and combination regimens (6, 27, 39).

Our study extends the existing evidence base twofold: firstly, by directly comparing the impact of csDMARD use across adalimumab and secukinumab within the same cohort, demonstrating a significant interaction effect that supports drug-specific treatment strategies. This direct within-cohort comparison avoids the methodological limitations inherent to indirect comparisons across different studies. Secondly, our study includes data not only on MTX combination treatment, but also on LEF and combinations of multiple csDMARDs, further broadening the clinical relevance of our findings.

Exploratory analysis suggested that for adalimumab, both MTX-based and LEF-based combination therapy were associated with longer drug retention compared to monotherapy, while no clear difference between MTX-based and LEF-based regimens was observed (Supplementary Figure S2a). However, an inherent limitation of this comparison is that LEF is frequently used as a second-choice csDMARD in patients who have failed or are intolerant to MTX, meaning the LEF combination group likely represents a more refractory patient population. These findings suggest that the benefit of combination therapy for adalimumab retention may not be specific to MTX, but rather reflect a broader effect of concomitant csDMARD use regardless of agent. This is in contrast with the ATTRA registry in RA patients, demonstrating superior TNFi retention specifically for MTX over other csDMARDs (22). Nevertheless, the statistical power to reliably confirm or refute a differential effect between MTX and LEF remains

insufficient of our data. The mechanisms underlying the combination benefit for adalimumab specifically may relate to MTX's more potent suppression of ADA and improvement of serum trough levels (40).

Strengths of this study include its real-world clinical setting, extensive follow-up, large cohort of PsA patients, and direct within-cohort comparison of the most commonly prescribed representatives of the TNFi and IL-17i classes. We also evaluated several potential clinical confounders, including prior csDMARD exposure, prior b/tsDMARD use, and disease duration. As these variables showed substantial collinearity with age, the final models were adjusted for age and sex only. The per-protocol sensitivity analysis further strengthened our conclusions by accounting for changes in concomitant csDMARD use over time. Several limitations warrant consideration. First, the retrospective nature of this study precludes random treatment allocation, introducing confounding by indication. The decision to prescribe concomitant csDMARD therapy was at the physician's discretion, likely influenced by unmeasured clinical factors. Second, the retrospective design resulted in missing data, and as disease activity measures were not consistently available for all patients at baseline and follow-up, we were unable to assess treatment response beyond drug retention, introducing potential information bias. Finally, as this was a single-center multi-location study conducted in the Netherlands, generalizability to other healthcare settings should be considered with caution.

Given the monitoring burden, potential toxicity, and costs associated with csDMARDs, our results support a more individualized approach to combination therapy in PsA. For patients initiating adalimumab, continuation of existing csDMARD therapy appears beneficial. Conversely, for patients initiating secukinumab, our findings suggest no added value of csDMARD co-medication for drug retention. Indeed, discontinuation of the csDMARD when initiating secukinumab may be the best approach for the patient. This approach could reduce treatment burden, healthcare costs, and adverse effect risks without compromising drug retention. However, this recommendation applies specifically to drug retention as an outcome; the potential impact on other clinical endpoints including joint damage progression, achievement of minimal disease activity, and patient-reported outcomes warrant further investigation.

Conclusion

In conclusion, this cohort study demonstrates that concomitant csDMARD use significantly prolongs drug retention for adalimumab but not for secukinumab in PsA patients. The significant interaction between bDMARD type and csDMARD use indicates that treatment strategies should be tailored according to the specific bDMARD. Therefore, csDMARDs should be continued when initiating adalimumab, but may be discontinued when starting secukinumab. Further prospective research is warranted to explore effectiveness of bDMARD with and without csDMARD use in terms of disease activity, to clarify underlying mechanisms, and guide optimized patient-tailored treatment strategies in psoriatic arthritis.

Abbreviations

ACR
American College of Rheumatology
Anti-CCP
Anti-citrullinated protein
ADA
Anti-drug antibody
bDMARD
Biologic disease-modifying antirheumatic drugs
BMI
Body mass index
CRP
C-reactive protein
csDMARD
Conventional synthetic disease-modifying antirheumatic drugs
DAS28-CRP
Disease Activity Score 28 with CRP
DMARD
Disease-modifying antirheumatic drugs
EULAR
International European Alliance of Associations for Rheumatology
GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
HR
Hazard ratio
IL-17i
Interleukin-17 inhibitors
IRIS
Integrated Rheumatology Information System
IQR
Interquartile range
MTX
Methotrexate
NSAID
Non-steroidal anti-inflammatory drugs
LEF
Leflunomide
PsA
Psoriatic arthritis
RA
Rheumatoid arthritis

RF
Rheumatoid factor
SJC
Swollen joint score
TJC
Tender joint score
TNFi
Tumor necrosis factor inhibitors
VAS
Visual analog scale for patient global assessment

Declarations

Ethics approval and consent to participate: The study was in accordance with the Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects. Ethical approval was not required, as assessed by the local ethics committee (Commissie Mensgebonden Onderzoek region Arnhem-Nijmegen, 2023-16716). Patients who did not object against the use of clinical data for research purposes were included. This is in line with local law and guidelines.

Consent for publication: Not applicable.

Availability of data and materials: The participants in this study did not give written consent for their data to be shared publicly. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions: SG analyzed the data, performed data curation, validation, and visualization, and wrote the original manuscript. EM, JV, NvH, AdB and IvdHB contributed to the methodology and critically revised the manuscript. NdB and EL contributed to the conceptualization, data curation, methodology,

and project administration, supervised the study, and critically revised the manuscript. All authors read and approved the final manuscript.

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Figures

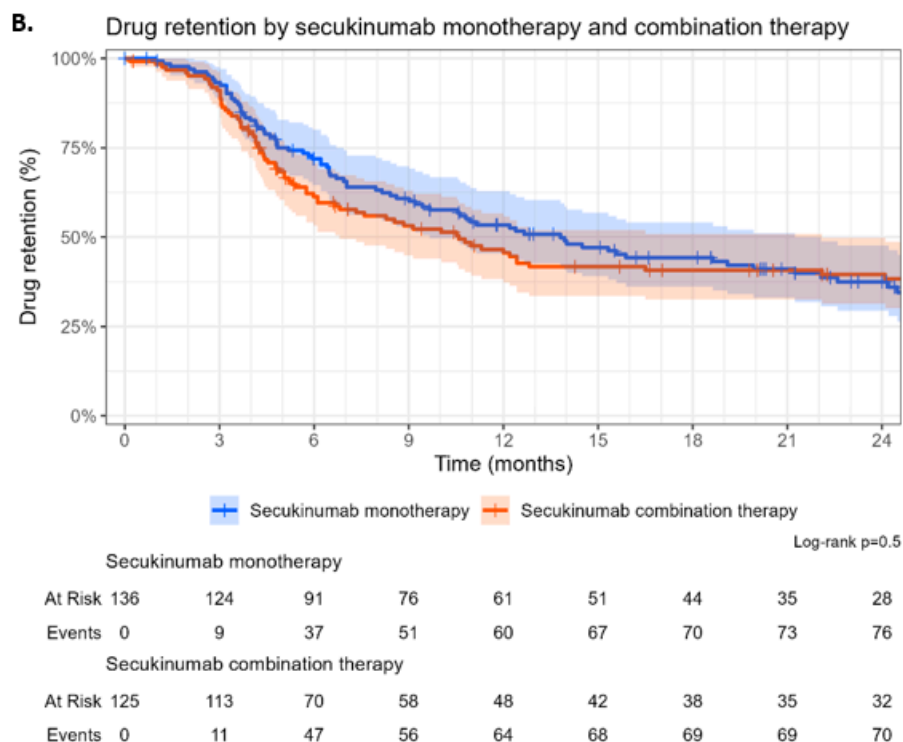
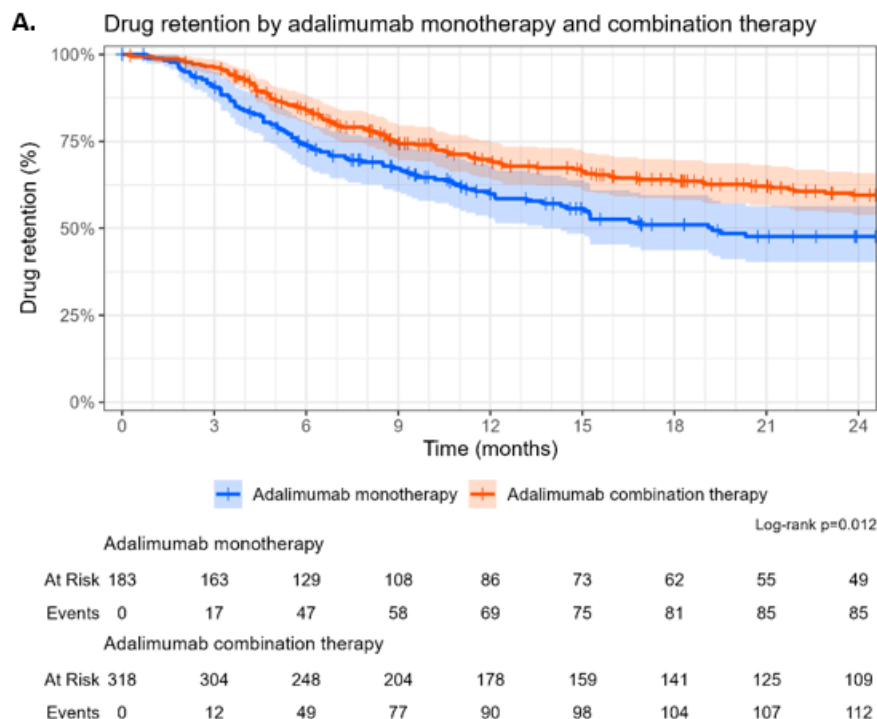


Figure 1

Kaplan–Meier curves of retention for adalimumab and secukinumab monotherapy versus combination therapy. Drug retention in patients treated with (A) adalimumab monotherapy versus combination therapy and (B) secukinumab monotherapy versus combination therapy. Kaplan–Meier curves illustrate drug retention for each treatment strategy, with shaded areas representing 95% confidence intervals. Numbers at risk and cumulative events are shown below the plots.

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