Durability of Response Among Patients with Psoriatic Arthritis (PsA) Using Biological or Targeted Synthetic Disease-Modifying Antirheumatic Drugs in the CorEvitas PsA/Spondyloarthritis Registry

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Objective

This study aimed to describe the durability of treatment response over 24 months following achievement of 50% improvement in the modified American College of Rheumatology response (mACR50), and factors associated with the response, among patients in the CorEvitas Psoriatic Arthritis (PsA)/Spondyloarthritis (SpA) Registry treated with biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).

Background

- PsA is a chronic inflammatory disease affecting both the joints and skin; control of the disease is a challenging, yet important treatment goal.[1]
- Current guidelines recommend advanced therapy when PsA is not adequately controlled with conventional DMARDs (cDMARDs); however, despite an initial response to advanced therapy, many patients fail to maintain the response over time, demonstrating a significant unmet need.[1]
- Our understanding of durability of response to b/tsDMARD therapy among PsA patients, as well as patient characteristics that might impact durability in a real-world setting, is limited.

Methods

- The CorEvitas PsA/SpA Registry is a prospective, observational North American research registry launched in 2013.
- PsA patients who initiated b/tsDMARDs ("treatment index") from March 2013–February 2022 and achieved mACR50 at 6 (±3) months post-initiation ("study start index") were followed until first occurrence of loss of response, last study visit, or 24 months post-achievement (**Figure 1**).
- Loss of treatment response was defined as earliest occurrence of b/tsDMARD discontinuation, non-biologic addition, or loss of mACR50.
- The mACR50 response measure, which did not require laboratory results, was validated to have high correlation with ACR50 in the CorEvitas registry.[2]
- Patient and clinical characteristics, including disease activity and patient-reported outcomes (PROs), were assessed at treatment index and time of mACR50 achievement.
- Percentage (95% confidence interval [CI]) of patients who maintained treatment response at 6, 12, 18, and 24 months were reported, in addition to median time to loss of response using a Kaplan-Meier Turnbull non-parametric survival method for interval censored outcomes.
- To identify risk factors associated with loss of treatment response, unadjusted proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% CIs for each factor.
- A multivariable adjusted model was built based on univariate results and clinical plausibility.

Results

Patient Demographics and Lifestyle Characteristics

- The study cohort included 189 b/tsDMARD initiations from 184 unique patients (**Table 1**).
- Mean (standard deviation [SD]) age was 53.0 (13.3) years, 52% of patients were female, 89% were White, 86% were overweight/obese, 58% of patients were biologic-naive, and 32% had no prior cDMARD history.
- Mean (SD) PsA disease duration was 5.9 (7.6) years, with 8.1 (9.3) years since symptom onset.

Durability of Response in the mACR50 Study Population

- At mACR50 achievement, improvements in disease activity and PROs from b/tsDMARD initiation were observed. However, 8% of patients who achieved mACR50 still had moderate/high disease activity according to the Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA), and 20% had not reached minimal disease activity (MDA).
- Over the 24-month follow-up, 37% (95% CI: 31%, 43%) of initiators lost response at 6 months, 52% (95% CI: 45%, 58%) at 12 months, 68% (95% CI: 62%, 73%) at 18 months, and 70% (95% CI: 65%, 75%) at 24 months (**Figure 2**). Median time to loss of mACR50 response was 9.3 months (95% CI: 7.5, 13.0; **Table 2**).
- Among those who were persistent on therapy, approximately 30% (n=55) of initiators maintained treatment response at the last visit, while 57% (n=108) had loss of mACR50 (**Table 3**).
- Multivariable-adjusted analysis demonstrated that higher EuroQol-5D (EQ-5D) score at initial achievement of mACR50 (0.1 unit increase, HR=0.8 [95% CI: 0.67, 0.96]) and having a college education (HR=0.5 [95% CI: 0.30, 0.83]) were associated with lower risk of mACR50 loss (**Figure 3**).

Conclusions

Among real-world patients with PsA who achieved mACR50 after b/tsDMARD initiation, approximately one-third lost treatment response at 6 months, half at 12 months, and two-thirds at 18- and 24-months post-achievement.

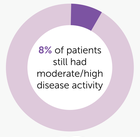
A higher EQ-5D score and college education, denoting greater health status and educational background, was associated with longer durability of mACR50, following the initial response.

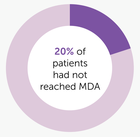
These findings suggest that rheumatologists may consider addressing persistent patient-reported symptoms and quality of life at achievement of treatment response to reduce the likelihood of loss of response to advanced therapy.

Summary

This study evaluated durability of treatment response among PsA patients who initiated b/tsDMARDs and achieved mACR50 after 6 (±3) months

At achievement of mACR50:





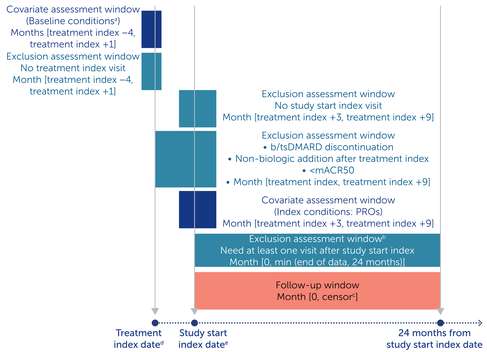
After initial mACR50 response:

37% of patients lost treatment response at 6 months, **52%** at 12 months, and **70%** at 24 months after initial response.

A **higher EQ-5D** score and **college education** were associated with **longer durability** of mACR50.

Clinical implications
Rheumatologists may consider addressing persistent patient-reported symptoms and quality of life at achievement of treatment response to reduce the likelihood of loss of response.

Figure 1 Study design



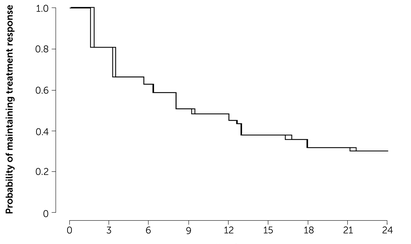
Registry treatment index visit corresponds to biologic initiation study visit; study start index visit corresponds to the study visit 6 months after baseline. The study start index visit could occur in a window of 3–9 months and was defined as the first study visit if multiple study visits occurred in the window. [a] Included sociodemographic characteristics, history of comorbidities, PsA disease characteristics, PsA activity measures, previous and current medications. [b] Bias analysis was conducted in the sensitivity analysis to assess the impact of exclusion; [c] Censor: any loss of treatment response, last follow-up visit, or 24 months after study start index date, whichever was soonest; [d] Date of initiation of approved b/tsDMARDs; [e] Achieved mACR50 response level.

Table 1 Demographic and lifestyle characteristics for all PsA patients in the CorEvitas PsA/SpA Registry who initiated b/tsDMARD treatment

	At treatment index (N=189)	At study start index[a] (N=189)
Demographic characteristics		
Age, mean (SD)	53.0 (13.3)	53.6 (13.2)
Female, n (%)	99 (52.4%)	99 (52.4%)
Race (White), n (%)	162 (88.5%)	162 (88.5%)
College education, n (%)	142 (75.5%)	142 (75.5%)
Work full-time, n (%)	114 (60.6%)	112 (59.6%)
Lifestyle characteristics		
BMI, n (%)		
Overweight (25–30)	52 (28.0%)	55 (29.6%)
Obese (>30)	107 (57.5%)	105 (56.5%)
Disease characteristics		
History of comorbidities, n (%)		
CVD	20 (10.6%)	20 (10.6%)
Malignancy	14 (7.4%)	14 (7.4%)
Depression	26 (13.8%)	27 (14.3%)
Anxiety	16 (8.5%)	16 (8.5%)
Hypertension	79 (41.8%)	79 (41.8%)
Diabetes	23 (12.2%)	23 (12.2%)
Duration of PsA symptoms (years), mean (SD)	8.1 (9.3)	8.7 (9.2)
Spinal involvement, n (%)	17 (9.0%)	11 (5.8%)
Age at PsA onset, mean (SD)	45.0 (13.2)	45.0 (13.2)
Disease activity		
Tender joint count (0–68), mean (SD)	8.6 (9.6)	0.8 (1.9)
Swollen joint count (0–66), mean (SD)	5.9 (6.4)	0.6 (1.8)
Dactylitis, n (%)	61 (32.3%)	10 (5.3%)
cDAPSA category, n (%)		
Remission (0–4)	1 (0.5%)	105 (56.5%)
Low disease activity (>4–13)	41 (22.0%)	66 (35.5%)
Moderate disease activity (>13–27)	91 (48.9%)	14 (7.5%)
High disease activity (>27)	53 (28.5%)	1 (0.5%)
MDA, n (%)	18 (9.7%)	145 (79.7%)
PROs		
HAQ-DI, mean (SD)	0.8 (0.6)	0.3 (0.4)
Pain (VAS-100), mean (SD)	51.4 (26.3)	18.1 (19.4)
Spine pain (VAS-100), mean (SD)	24.5 (27.8)	12.2 (18.7)
Patient global assessment of arthritis (VAS-100), mean (SD)	40.6 (24.6)	17.5 (21.2)
Fatigue (VAS-100), mean (SD)	46.2 (27.1)	25.5 (24.5)
Morning stiffness (VAS-100), mean (SD)	53.0 (28.2)	19.6 (20.6)
EQ-5D, mean (SD)	0.7 (0.2)	0.8 (0.1)
Treatment characteristics		
b/tsDMARD at initiation, n (%)		
TNFi	106 (56.7%)	106 (56.7%)
IL-17i	48 (25.7%)	48 (25.7%)
IL-23i	3 (1.6%)	3 (1.6%)
IL-12/23i	12 (6.4%)	12 (6.4%)
JAKi	7 (3.7%)	7 (3.7%)
Apremilast	11 (5.9%)	11 (5.9%)
Combination therapy with cDMARD	65 (34.4%)	65 (34.4%)
Prior b/tsDMARDs, n (%)		
0	110 (58.2%)	95 (50.3%)
1	62 (32.8%)	77 (40.7%)
2+	17 (9.0%)	17 (9.0%)
Prior cDMARDs, n (%)		
0	61 (32.3%)	61 (32.3%)
1	104 (55.0%)	104 (55.0%)
2+	24 (12.7%)	24 (12.7%)
Current NSAID use, n (%)	58 (30.7%)	162 (85.7%)

[a] At achievement of mACR50.

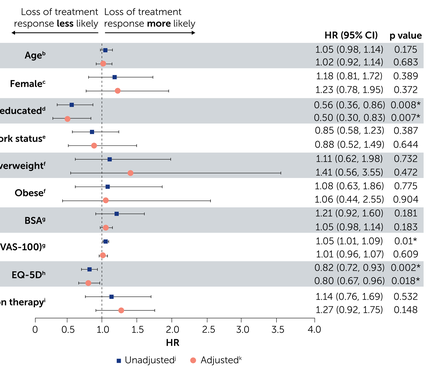
Figure 2 Kaplan-Meier curve reporting probability of maintaining mACR50 treatment response over 24 months



Months	0	3	6	9	12	15	18	21	24
Number remaining at risk (n)	189	185	155	122	110	92	82	76	72

N=189. Calculation of the mACR50 response correlates with calculation of the ACR50 response, but with the removal of laboratory measures (ESR and CRP). Time to loss of response was not known precisely; intervals are denoted with an additional line.

Figure 3 Association between loss of treatment response and patient and disease characteristics at study start index[a]



*Significance level set at p<0.05. [a] At achievement of mACR50; [b] 5-year increase; [c] Reference: male; [d] Reference: no college education; [e] Reference: not working full-time; [f] According to BMI (Reference: underweight/normal); [g] Reference: 5-unit increase; [h] Reference: 0.1-unit increase; [i] Combination therapy with cDMARD (reference: monotherapy); [j] Univariate model where each predictor was tested one at a time; [k] Models were adjusted for age, sex, college education, work status, BMI, BSA, fatigue, EQ-5D, and combination therapy; model variables were selected based on univariate regression results and clinical knowledge.

Table 2 Description of time until loss of mACR50 treatment response

	Months (95% CI) to loss of response			Percent (95% CI) maintaining treatment response			
	25th percentile	Median	75th percentile	6 months	12 months	18 months	24 months
All initiators (N=189)	3.4 (1.8, 3.7)	9.3 (7.5, 13)	NA (21.6, NA)	62.8 (56.6, 69.3)	48.1 (42.1, 54.5)	31.9 (26.7, 37.7)	30.1 (24.8, 35.2)

NA: As 30% maintained response at 24 months (the end of follow-up), the 75th percentile of time to loss of response could not be calculated.

Table 3 Frequencies of first occurrence of b/tsDMARD persistence, discontinuation, start of a new non-biologic therapy, and loss of mACR50 response within 24 months of study start index date after achieving mACR50

	n (%)[a]	Months from study start index data, median (IQR)[b]
No loss of treatment response		
Persistent	55 (29.1%)	-
Non-failure discontinuation		
Temporary discontinuation	1 (0.5%)	18.0 (18.0, 18.0)
Other[c]	0 (0.0%)	-
Loss of treatment response		
Failure discontinuation	23 (12.2%)	7.4 (5.0, 15.9)
Side effect (minor, serious)	1 (0.5%)	12.2 (12.2, 12.2)
Failure to maintain initial response	1 (0.5%)	5.6 (5.6, 5.6)
Missing reason	21 (11.1%)	7.4 (4.6, 16.1)
Other[d]	0 (0.0%)	-
Start of new systemic non-biologic therapy	2 (1.1%)	6.7 (4.0, 9.4)
Loss of mACR50	108 (57.1%)	0.0 (0.0, 6.2)

[a] Percentages based on all initiators (N=189); [b] Median and IQR are reported using the lower bound in patients that have an interval censored time until loss of treatment response; [c] Includes patient request, administrative reason, fear of future side effect, and drug administration discontinuations; [d] Includes improving compliance/tolerability, inadequate initial response, alternative mechanism of action, and active disease.

ACR50: 50% improvement in the American College of Rheumatology response; **BMI:** body mass index; **BSA:** body surface area; **b/tsDMARD:** biological/targeted synthetic disease-modifying antirheumatic drug; **cDAPSA:** Clinical Disease Activity Index for Psoriatic Arthritis; **cDMARD:** conventional disease-modifying antirheumatic drug; **CI:** confidence interval; **CRP:** C-reactive protein; **CVD:** cerebro–cardiovascular disease; **ESR:** erythrocyte sedimentation rate; **EQ-5D:** EuroQol-5D; **HAQ-DI:** Health Assessment Questionnaire Disability Index; **HR:** hazard ratio; **i:** inhibitor; **IL:** interleukin; **IQR:** interquartile range; **JAK:** Janus kinase inhibitor; **mACR50:** 50% improvement in the modified American College of Rheumatology response; **MDA:** minimal disease activity; **NSAID:** nonsteroidal anti-inflammatory drug; **PRO:** patient-reported outcome; **PsA:** psoriatic arthritis; **SD:** standard deviation; **SpA:** spondyloarthritis; **TNF:** tumor necrosis factor; **VAS:** visual analog scale.

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References: Gossec L. Ann Rheum Dis 2020;79:700–712; Greenberg JD. Rheumatol 2009;48:686–690. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AO, CS, NM, MM, ME, SWB, RL, PJM;** drafting of the publication, or reviewing it critically for important intellectual content: **AO, CS, NM, MM, ME, SWB, RL, PJM;** final approval of the publication: **AO, CS, NM, MM, ME, SWB, RL, PJM.** **Author Disclosures: AB:** Grant/research support to the University of Pennsylvania from AbbVie, Janssen, Novartis and Pfizer; Grant/research support to Forward from Amgen; Consultant for AbbVie, Amgen, Bristol-Myers Squibb, Celgene, CorEvitas, Eli Lilly, Gilead, GSK, Janssen, Novartis, Pfizer and UCB Pharma; **CS, RL:** Employees and shareholders of UCB Pharma; **SWB:** Employee at the time of research and current shareholder of UCB Pharma; **NM, MM, ME:** Employees of CorEvitas, LLC; **PJM:** Has received research grants from AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; consulting fees from AbbVie, Acelyrin, Aclaris, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Moonlake Pharma, Novartis, Pfizer, Sun Pharma, and UCB Pharma; and speaker bureau fees from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma. **Acknowledgements:** This study was sponsored by CorEvitas, LLC. CorEvitas has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Inc., Arena, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Chugai, Eli Lilly and Company, Genentech, Gilead Sciences, Inc., GlaxoSmithKline, Janssen Pharmaceuticals, Inc., LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Inc., Regeneron Pharmaceuticals, Inc., Sanofi, Sun Pharmaceutical Industries Ltd., and UCB S.A. We would like to thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Quinn Ho, PhD, and Claire Hews, PhD, at Costello Medical (Boston, MA, US, and Cambridge, UK, respectively) for medical writing, and the Costello Medical Creative team for design support. All costs associated with development of this poster were funded by UCB Pharma.

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