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Combination Use of Systemic Therapies in Psoriasis: Baseline Characteristics from the Corrona Psoriasis Registry

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ABSTRACT

Importance: There are increasing options for systemic combination therapy for psoriasis but a lack of literature around the characteristics of patients who are started on these regimens.

Objective: We aimed to determine how combination systemic therapy patients differ from monotherapy patients in their social, medical, or treatment history.

Design: This was a cross-sectional study of patients enrolled in the Corrona Psoriasis Registry. Descriptive characteristics were compared in biologic monotherapy and combination therapy groups.

Setting: The Corrona PsO registry is a prospective multicenter observational disease-based registry with patients recruited from 154 private and academic practice sites in the US and Canada with 373 participating dermatologists.

Participants: Patients 18 years of age or older who enrolled in the Corrona Psoriasis Registry between April 2015 and March 2017 and initiated an eligible biologic therapy at the time of enrollment were included.

Exposures: Eligible biologic therapies included adalimumab, etanercept, infliximab, ixekizumab, secukinumab, and ustekinumab. Non-biologic and small molecule adjunctive therapies included acitretin, apremilast, CsA, and MTX.

Results: Patients on combination therapy were more likely to identify as black, to have Medicaid, and to report disabled work status. While combination therapy patients were more likely to have concomitant PsA, no major differences were seen in disease morphology, duration, IGA, PASI, or BSA affected at treatment initiation.

Conclusions: Various demographic and socioeconomic factors are associated with use of combination systemic therapy compared to use of systemic monotherapy for psoriasis. An association with commonly used disease severity indices was not observed.

Relevance: An understanding of which patients are more likely to be prescribed combination systemic therapy will provide important context for long-term efficacy and safety data as they become available.

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BACKGROUND

Treatment of moderate-to-severe psoriasis often poses a challenge to the physician.[1] Patients with widespread disease frequently fail to respond to initial topical treatments and phototherapy and quickly move to the next therapeutic step: single-agent systemic therapy. However, systemic monotherapy can be insufficient in attaining the desired level of control, and increasing the dose of many of the first-line medications may pose a safety risk to the patient. Combination therapies present another option in these difficult cases.[2]

Combination therapies for moderate-to-severe psoriasis may consist of two systemic agents or one systemic agent with topical or phototherapy. While there are numerous studies establishing the safety and efficacy of the latter, data regarding systemic combination therapy are limited. There is evidence that methotrexate (MTX) and cyclosporine (CsA) can be used together effectively.[3] However, both of these medications are associated with significant side effects and consistent monitoring is required throughout treatment. Newer therapies such as systemic retinoids, phosphodiesterase inhibitors, and biologic drugs have comparatively more favorable side effect profiles.[4] As such, physicians have begun to use these drugs in combination with traditional systemic agents and, in some cases, with one another.

There is a paucity of literature related to combination therapies involving these newer agents.[5] Initial investigations suggest that biologic drugs in combination with CsA, MTX, acitretin, or

even another biologic are promising options for plaque psoriasis.[6-8] However, the majority of these studies investigated only one class of biologic drugs: tumor necrosis factor (TNF)-alpha antagonists. The newer classes of biologic therapies (targeting IL-12/23, IL-17, and IL-23) may be even more favorable in combination therapy due to their improved safety profiles.[8] Additionally, all of these studies were focused on assessing safety and efficacy with very little data on the phenotypes most likely to be prescribed these regimens in the first place.

The Corrona Psoriasis Registry is an independent, prospective observational cohort launched in 2015 with an enrollment target of 12,000 psoriasis patients across the United States (US) and Canada. Corrona registries are designed to study real-world use of biologic therapies and have previously been used to analyze the safety and efficacy of combination therapies in rheumatologic disease.[9] While the average length of follow up for Psoriasis Registry subjects is not yet long enough to investigate the safety and efficacy of these regimens, there are sufficient data to conduct an initial analysis of baseline characteristics in this population. These characteristics include demographics, treatment history, disease characteristics and severity, comorbidities, and patient-reported outcomes (PROs). We hypothesize that patients placed on concurrent systemic therapies will differ from the single-agent therapy population in their social, medical, or treatment history. An understanding of which patients are more likely to be prescribed combination systemic therapy will provide important context for long-term efficacy and safety data as they become available.

METHODS

Study Setting

The Corrona PsO registry is a prospective multicenter observational disease-based registry launched in April 2015 in collaboration with the National Psoriasis Foundation (NPF). The registry design and patient enrollment has been previously described.[10] Briefly, patients were recruited from 154 private and academic practice sites in the US and Canada with 373 participating dermatologists. As of April 2018, Corrona's PsO database included information on approximately 2702 patients with 11553 patient visits, and 3892.3 patient-years of follow-up observation time had been collected. The mean time of patient follow-up was 1.36 years (median 1.28 years).

All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor approval and continuing review was obtained through a central IRB (IntegReview Institutional Review Board, Corrona-PSO-500). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRBs and documentation of approval was submitted to the Sponsor prior to initiating any study procedures. All registry subjects were required to provide written informed consent prior to participating.

Study Population

Patients 18 years of age or older who enrolled in the Corrona Psoriasis Registry between April 2015 and March 2017 and initiated an eligible biologic therapy at the time of enrollment were included. Patients were grouped into two mutually exclusive cohorts based on initial treatment regimen: biologic mono-therapy and biologic combination therapy. The combination therapy group consisted of patients beginning a new biologic adjunctively with a non-biologic systemic therapy. Biologic therapies included adalimumab, etanercept, infliximab, ixekizumab, secukinumab, and ustekinumab. Non-biologic and small molecule adjunctive therapies included acitretin, apremilast, CsA, and MTX.

Descriptive Characteristics

Demographics, clinical measures, and PROs were examined and compared between biologic mono-therapy and combination therapy groups at treatment initiation. Clinical measures included psoriasis duration and morphology, concomitant PsA, psoriasis area and severity index (PASI), investigator global assessment (IGA), body surface area (BSA) affected, and various comorbidities. PROs included Work Productivity and Activity Impairment (WPAI) scores, self-completed measure of health status (EQ-5D-3L), Dermatology Life Quality Index (DLQI), and overall fatigue, itch, and pain on a visual analogue scale (VAS) 0-100.

Statistical Analysis

Categorical variables were summarized using frequency counts and percentages; continuous variables were summarized by number of observations, mean, standard deviation, median, and the interquartile range (IQR). T-test and Wilcoxon rank sum test were employed for continuous variables and Chi-square of association for categorical variables to test for at least one significant difference across all categories of a variable.

RESULTS

Of the 2702 patients enrolled in the Registry through March 2017, 2189 were on eligible biologic therapies at registry enrollment. Of those, 842 patients initiated treatment at enrollment, with 750 (89%) on systemic mono-therapy and 92 (11%) on systemic combination therapy. Several demographic differences were observed between these two groups (Table 1). Patients on combination therapy were older (mean age 53.0 vs 48.6, P=0.007) and more likely to identify as black (10% vs 4%, P=0.048). The combination therapy group was also more likely to have Medicaid (20% vs 7%, P<0.001) and to report disabled work status (16% vs 7%, P=0.014). A greater percentage of combination therapy patients had Medicare, although the difference was not statistically significant (20% vs 15%, P=0.246).

TABLE 1.

Patient Demographics at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy

Disease Characteristics	Total N=842	Biologic Combo-Therapy N=92	Biologic Mono-Therapy N=750	*P*-Value
Age (yrs), *mean (SD)*	n=842 49.1 (14.7)	n=92 53.0 (13.9)	n=750 48.6 (14.7)	0.007
Age categorical, *n (%)*:	n=842	n=92	n=750	0.183
18-29	99 (12%)	4 (4%)	95 (13%)	
30-39	145 (17%)	13 (14%)	132 (18%)	
40-49	159 (19%)	19 (21%)	140 (19%)	
50-59	224 (27%)	28 (30%)	196 (26%)	
60-69	149 (18%)	18 (20%)	131 (17%)	
70+	66 (8%)	10 (11%)	56 (7%)	
Sex, *n (%)*	n=842	n=92	n=750	0.585
Male	407 (48%)	42 (46%)	365 (49%)	
Female	435 (52%)	50 (54%)	385 (51%)	
Race, *n (%)*	n=842	n=92	n=750	0.048
White	699 (83%)	71 (77%)	628 (84%)	
Black	36 (4%)	9 (10%)	27 (4%)	
Asian	57 (7%)	7 (8%)	50 (7%)	
Other*	50 (6%)	5 (5%)	45 (6%)	
Ethnicity, *n (%)*	n=838	n=90	n=748	0.273
Hispanic	61 (7%)	4 (4%)	57 (8%)	
Body height (*m*), *mean (SD)*	n=839 1.7 (0.1)	n=92 1.7 (0.1)	n=747 1.7 (0.1)	0.116
Body weight (kg), *mean (SD)*	n=837 90.7 (23.4)	n=92 89.9 (22.2)	n=745 90.8 (23.6)	0.726
BMI (kg/m^2), *mean (SD)*	n=836 31.0 (7.4)	n=92 31.3 (7.0)	n=744 31.0 (7.4)	0.701
BMI categorical, *n (%)*	n=836	n=92	n=744	0.798
Normal/Underweight (<25)	177 (21%)	17 (18%)	160 (22%)	
Overweight (25.0<30)	230 (28%)	26 (28%)	204 (27%)	
Obese (≥30)	429 (51%)	49 (53%)	380 (51%)	
Insurance Type, *n (%)* **	n=842	n=92	n=750	
Private	666 (79%)	66 (72%)	600 (80%)	0.066
Medicare	130 (15%)	18 (20%)	112 (15%)	0.246
Medicaid	69 (8%)	18 (20%)	51 (7%)	<0.001
No Insurance	29 (3%)	1 (1%)	28 (4%)	0.189
Education, *n (%)*	n=842	n=92	n=750	0.680
12th grade or less	52 (6%)	6 (7%)	46 (6%)	
High school graduate/GED	188 (22%)	25 (27%)	163 (22%)	
Some college/Assoc. degree	271 (32%)	27 (29%)	244 (33%)	
College graduate or higher	331 (39%)	34 (37%)	297 (40%)	
Work Status, *n (%)*	n=842	n=92	n=750	0.014
Full time	499 (59%)	49 (53%)	450 (60%)	
Part time	75 (9%)	8 (9%)	67 (9%)	
Work at home	56 (7%)	5 (5%)	51 (7%)	
Student	27 (3%)	0 (0%)	27 (4%)	
Disabled	65 (8%)	15 (16%)	50 (7%)	
Retired	120 (14%)	15 (16%)	105 (14%)	

TABLE 1. (CONTINUED)

Patient Demographics at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy				
Disease Characteristics	**Total N=842**	**Biologic Combo-Therapy N=92**	**Biologic Mono-Therapy N=750**	***P*-Value**
Alcohol Use History***, *n (%)*	n=831	n=91	n=740	0.224
Non-Drinker	263 (32%)	36 (40%)	227 (31%)	
Casual	417 (50%)	41 (45%)	376 (51%)	
Daily	151 (18%)	14 (15%)	137 (19%)	
Smoking, *n (%)*	n=838	n=92	n=746	0.964
Current smoker	158 (19%)	18 (20%)	140 (19%)	
Former smoker	283 (34%)	30 (33%)	253 (34%)	
Never smoked	397 (47%)	44 (48%)	353 (47%)	
Population Regions****, *n (%)*	n=842	n=92	n=750	0.224
Northeast	302 (36%)	25 (27%)	277 (37%)	
Midwest	111 (13%)	15 (16%)	96 (13%)	
South	341 (40%)	39 (42%)	302 (40%)	
West	88 (10%)	13 (14%)	75 (10%)	

*Other race includes Native American, Native Hawaiian or other Pacific Islander, and Other.
**Insurance categories may overlap.
***Alcohol use based on average drinks per day [Quantity*Frequency] over the past year with daily drinkers (average of 1 drink per day) representing the upper quartile of drinkers (ie, 75-percentile).
****Regional divisions based on the United States Census Bureau: Northeast – MA, RI, NH, CT, VT, ME, NY, NJ, PA; Midwest – IN, IL, OH, MI, WI, MN, IA, MO, ND, SD, NE, KS; South – MD, DE, DC, VA, WV, NC, SC, GA, FL, LA, AR, OK, TX, MS, AL, TN, KY; West – AZ, CO, ID, NM, MT, UT, NV, WY, AK, CA, HI, OR, WA.

TABLE 2.

Disease Characteristics at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy				
Disease Characteristics	**Total N=842**	**Biologic Combo-Therapy N=92**	**Biologic Mono-Therapy N=750**	***P*-Value**
Years Since Diagnosis				
Psoriasis duration (yrs), *n*	n=841	n=92	n=749	0.948
mean (SD)	15.5 (13.9)	15.4 (14.8)	15.5 (13.8)	
median (IQR)	12.0 (4.0,24.0)	11.0 (3.0,24.0)	12.0 (4.0,24.0)	
Psoriatic Arthritis, *n (%)*	n=842	n=92	n=750	<0.001
Yes	320 (38%)	52 (57%)	268 (36%)	
Psoriatic Arthritis duration (yrs), *n*	n=320	n=52	n=268	0.777
mean (SD)	7.6 (9.0)	8.0 (9.7)	7.6 (8.9)	
median (IQR)	5.0 (1.0,11.0)	4.5 (1.5,11.0)	5.0 (1.0,11.5)	
IGA, *n**	n=841	n=92	n=749	0.550
mean (SD)	2.9 (0.8)	3.0 (0.9)	2.9 (0.8)	
median (IQR)	3.0 (3.0,3.0)	3.0 (3.0,4.0)	3.0 (3.0,3.0)	
IGA Categorical, *n (%)*	n=841	n=92	n=749	0.478
0: Clear	20 (2%)	3 (3%)	17 (2%)	
1: Almost clear	19 (2%)	2 (2%)	17 (2%)	
2: Mild	142 (17%)	15 (16%)	127 (17%)	
3: Moderate	488 (58%)	47 (51%)	441 (59%)	
4: Severe	172 (20%)	25 (27%)	147 (20%)	
BSA (% Involvement), *n***	n=839	n=91	n=748	0.056
mean (SD)	15.8 (17.3)	19.1 (22.5)	15.4 (16.5)	
median (IQR)	10.0 (5.0,20.0)	10.0 (4.0,22.0)	10.0 (5.0,20.0)	

TABLE 2. (CONTINUED)

Disease Characteristics at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy				
Disease Characteristics	**Total N=842**	**Biologic Combo-Therapy N=92**	**Biologic Mono-Therapy N=750**	***P*-Value**
BSA categorical % involvement, *n(%)*	n=839	n=91	n=748	0.338
Mild disease [0,3)	82 (10%)	11 (12%)	71 (9%)	
Moderate disease [3,10]	391 (47%)	36 (40%)	355 (47%)	
Severe disease (10,100]	366 (44%)	44 (48%)	322 (43%)	
PASI (Score: 0-77), *n*[***]	n=840	n=91	n=749	0.259
mean (SD)	9.4 (8.7)	8.4 (7.6)	9.5 (8.8)	
median (IQR)	7.2 (3.6,12.0)	6.0 (3.6,10.2)	7.2 (3.6,12.0)	
PASI>10, n (%)	n=840	n=91	n=749	0.097
Yes	287 (34%)	24 (26%)	263 (35%)	
History of Comorbidities[****]				
CVD, *n (%)*	29 (3%)	4 (4%)	25 (3%)	0.615
Hypertension, *n (%)*	312 (37%)	39 (42%)	273 (37%)	0.274
Hyperlipidemia, *n (%)*	221 (26%)	26 (28%)	195 (26%)	0.658
Diabetes Mellitus, *n (%)*	115 (14%)	17 (18%)	98 (13%)	0.158
Lymphoma/Malignancy, *n (%)*	1 (0%)	1 (1%)	0 (0%)	0.110
Metabolic Syndrome, *n (%)*	13 (2%)	0 (0%)	13 (2%)	0.202
Crohn's Disease, *n (%)*	6 (1%)	0 (0%)	6 (1%)	0.388
Depression, *n (%)*	178 (21%)	22 (24%)	156 (21%)	0.502
Anxiety, *n (%)*	186 (22%)	23 (25%)	163 (22%)	0.488
History of PsO Morphology				
Plaque, *n (%)*	816 (97%)	88 (96%)	728 (97%)	0.459
Guttate, *n (%)*	44 (5%)	5 (5%)	39 (5%)	0.924
Erythrodermic, *n (%)*	40 (5%)	6 (7%)	34 (5%)	0.397
Pustular (localized), *n (%)*	11 (1%)	1 (1%)	10 (1%)	0.844
Pustular (generalized), *n (%)*	3 (27%)	0 (0%)	3 (30%)	0.521
Inverse/Intertriginous, *n (%)*	64 (8%)	5 (5%)	59 (8%)	0.406
Scalp, *n (%)*	318 (38%)	29 (32%)	289 (39%)	0.190
Nail, *n (%)*	141 (17%)	13 (14%)	128 (17%)	0.477
Palmoplantar, *n (%)*	101 (12%)	13 (14%)	88 (12%)	0.504

[*]IGA: Investigator Global Assessment
[**]BSA: Body Surface Area
[***]PASI: Psoriasis Area and Severity Index
[****]History of comorbidities. CVD: Revascularization procedures (CABG, stent, angioplasty), Ventricular arrhythmia, Cardiac arrest, Acute coronary syndrome, Coronary artery disease, Transient ischemic attack, Hemorrhage with/without hospitalization (serious bleed), Deep vein thrombosis, Peripheral arterial disease, Pulmonary embolism, Carotid artery disease. Malignancy: Breast, Lung, Skin (excluding non-melanoma skin cancer) & Other.

TABLE 3.

Patient Reported Outcomes at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy				
Patient Reported Outcomes	**Total N=842**	**Biologic Combo-Therapy N=92**	**Biologic Mono-Therapy N=750**	***P*-Value**
WPAI Summary Scores	**n=842**	**n=92**	**n=750**	**0.167**
Currently employed, n (%)	575 (68%)	57 (62%)	518 (69%)	
Percent of work hours missed due to psoriasis, *n*	n=521	n=52	n=469	0.048
mean (SD)	4.6 (14.2)	8.3 (22.1)	4.2 (13.0)	
median (IQR)	0.0 (0.0,0.0)	0.0 (0.0,0.0)	0.0 (0.0,0.0)	
Percent of impairment while working due to psoriasis, *n*	n=517	n=50	n=467	0.128
mean (SD)	17.5 (23.8)	12.6 (22.8)	18.0 (23.8)	
median (IQR)	5.0 (0.0,25.0)	0.0 (0.0,11.0)	5.0 (0.0,25.0)	
Overall % of work hours affected by psoriasis, *n*	n=516	n=50	n=466	0.271
mean (SD)	19.5 (25.3)	15.8 (24.7)	19.9 (25.4)	
median (IQR)	9.8 (0.0,30.0)	2.0 (0.0,23.8)	10.0 (0.0,30.0)	
Percent of daily activities impaired by psoriasis, *n*	n=835	n=92	n=743	0.079
mean (SD)	25.5 (29.3)	30.6 (32.7)	24.9 (28.9)	
median (IQR)	10.0 (0.0,50.0)	15.0 (0.0,55.0)	10.0 (0.0,45.0)	
Patient health state today (EQ-5D VAS range 0-100), *n*	n=840	n=92	n=748	0.286
mean (SD)	68.7 (23.6)	66.2 (21.9)	69.0 (23.8)	
median (IQR)	75.0 (53.0,85.0)	70.0 (50.0,80.0)	75.0 (55.0,88.0)	
DLQI (Score: 0-30), *n*[***]	n=841	n=92	n=749	0.369
mean (SD)	9.3 (6.3)	8.7 (6.5)	9.3 (6.3)	
median (IQR)	8.0 (4.0,14.0)	7.0 (3.0,13.0)	8.0 (4.0,14.0)	
DLQI "Effect on life", *n (%)*	n=841	n=92	n=749	0.299
0-1: None	72 (9%)	12 (13%)	60 (8%)	
2-5: Small	205 (24%)	25 (27%)	180 (24%)	
6-10: Moderate	249 (30%)	21 (23%)	228 (30%)	
11-20: Very large	254 (30%)	29 (32%)	225 (30%)	
21-30: Extremely large	61 (7%)	5 (5%)	56 (7%)	
Patient overall fatigue (VAS range 0-100), *n*	n=840	n=92	n=748	0.037
mean (SD)	38.9 (30.4)	45.1 (31.5)	38.1 (30.2)	
median (IQR)	35.0 (10.0,65.0)	47.5 (15.0,75.0)	35.0 (10.0,62.5)	
Patient overall pain (VAS range 0-100), *n*	n=840	n=92	n=748	0.119
mean (SD)	38.8 (33.7)	33.7 (32.2)	39.5 (33.8)	
median (IQR)	30.5 (5.0,70.0)	25.0 (2.0,60.0)	34.0 (5.0,70.0)	
Patient overall itch (VAS range 0-100), *n*	n=841	n=92	n=749	0.051
mean (SD)	55.4 (33.6)	49.0 (33.3)	56.2 (33.5)	
median (IQR)	62.0 (20.0,85.0)	52.5 (15.0,78.5)	65.0 (25.0,85.0)	

TABLE 3. (CONTINUED)

Patient Reported Outcomes at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy				
Patient Reported Outcomes	**Total N=842**	**Biologic Combo-Therapy N=92**	**Biologic Mono-Therapy N=750**	***P*-Value**
Patient health state today (EQ VAS 0-100), *n*	n=840	n=92	n=748	0.286
mean (SD)	68.7 (23.6)	66.2 (21.9)	69.0 (23.8)	
median (IQR)	75.0 (53.0,85.0)	70.0 (50.0,80.0)	75.0 (55.0,88.0)	
EQ-5D-3L categorical domains**				
Walking, *n (%)*	n=838	n=92	n=746	0.114
No problems	620 (74%)	60 (65%)	560 (75%)	
Some problems	217 (26%)	32 (35%)	185 (25%)	
Bed ridden	1 (0%)	0 (0%)	1 (0%)	
Self-care, *n (%)*	n=831	n=92	n=739	0.233
No problems	745 (90%)	78 (85%)	667 (90%)	
Some problems	85 (10%)	14 (15%)	71 (10%)	
Unable to do	1 (0%)	0 (0%)	1 (0%)	
Usual activities, *n (%)*	n=832	n=92	n=740	0.038
No problems	548 (66%)	50 (54%)	498 (67%)	
Some problems	263 (32%)	38 (41%)	225 (30%)	
Unable to do	21 (3%)	4 (4%)	17 (2%)	
Pain & discomfort, *n (%)*	n=835	n=92	n=743	0.126
No problems	336 (40%)	28 (30%)	308 (41%)	
Some problems	430 (51%)	55 (60%)	375 (50%)	
Extreme problems	69 (8%)	9 (10%)	60 (8%)	
Anxiety & depression, *n (%)*	n=832	n=92	n=740	0.362
No problems	563 (68%)	60 (65%)	503 (68%)	
Some problems	244 (29%)	31 (34%)	213 (29%)	
Extreme problems	25 (3%)	1 (1%)	24 (3%)	

**EQ-*WPAI: Work Productivity & Activity Impairment Questionnaire (Scoring: http://www.reillyassociates.net/WPAI_Scoring.html);
**EQ-5D-3L: Self-completed measure of health status (Scoring: http://www.euroqol.org/about-eq-5d/how-to-use-eq-5d.html);
***DLQI: Dermatology Quality of Life Index (Scoring: http://sites.cardiff.ac.uk/dermatology/quality-of-life/dermatology-quality-of-life-index-dlqi/dlqi-instructions-for-use-and-scoring/).

With regard to baseline disease characteristics (Table 2), patients on combination therapy were more likely to have concomitant PsA (57% vs 36%, *P*<0.001). However, no other characteristics of their psoriatic disease differed significantly between the groups.

There were several notable differences in PROs (Table 3). The combination group experienced more overall fatigue, missed more hours from work, and had more problems performing activities of daily living. Table 4 details the treatment status and histories at enrollment for patients initiating biologic combination and mono-therapy. Combination therapy patients were much less likely to be naïve to non-biologic systemic medications; in other words, nearly all patients had tried a traditional systemic agent compared to only half of the mono-therapy group. No significant statistical difference was observed in treatment history with biologic drugs, including number of biologics tried and combination naivety.

TABLE 4.

Treatment Status and Histories at Biologic Initiation for Patients on Biologic Combo-Therapy and Mono-Therapy

Medication History [prior to registry enrollment]	Total N=842	Biologic Combo-Therapy N=92	Biologic Mono-Therapy N=750	*P*-Value
Biologic Naïve, *n (%)*	n=842	n=92	n=750	0.252
	330 (39%)	31 (34%)	299 (40%)	
Prior biologic usage count*,				
Count of patients: n (%)	n=512	n=61	n=451	0.408****
Count of drugs: median (IQR)	2.0 (1.0,3.0)	2.0 (1.0,3.0)	2.0 (1.0,2.0)	
Prior biologic counts given prior usage*, n (%)	n=512	n=61	n=451	0.678
1	240 (47%)	26 (43%)	214 (47%)	
2	143 (28%)	17 (28%)	126 (28%)	
3 or more	129 (25%)	18 (30%)	111 (25%)	
Non-biologic systemic naïve, *n (%)*	n=842	n=92	n=750	<0.001
	386 (46%)	2 (2%)	384 (51%)	
Prior non-biologic systemic usage count**,				
Count of patients: n (%)	n=456	n=90	n=366	0.207****
Count of drugs: median (IQR)	1.0 (1.0,2.0)	1.0 (1.0,2.0)	1.0 (1.0,2.0)	
Prior non-biologic counts given prior usage**, n (%)	n=456	n=90	n=366	0.296
1	314 (69%)	57 (63%)	257 (70%)	
2	103 (23%)	22 (24%)	81 (22%)	
3 or more	39 (9%)	11 (12%)	28 (8%)	
Biologic Combination naïve, *n (%)*	n=842	n=92	n=750	0.395
	762 (90%)	81 (88%)	681 (91%)	
Prior biologic combination usage count***,				
Count of patients: n (%)	n=80	n=11	n=69	0.187****
Count of drugs: median (IQR)	1.0 (1.0,1.0)	1.0 (1.0,2.0)	1.0 (1.0,1.0)	
Prior biologic combination therapy counts given prior usage***, n (%)	n=80	n=11	n=69	0.417
1	63 (79%)	7 (64%)	56 (81%)	
2	13 (16%)	3 (27%)	10 (14%)	
3 or more	4 (5%)	1 (9%)	3 (4%)	

*Prior Biologics include: adalimumab, alefacept, certolizumab, efalizumab, etanercept, golimumab, infliximab, secukinumab, ustekinumab, ixekizumab, investigational drugs, and other biologics.
**Prior Non-Biologic includes: acitretin, apremilast, cyclosporine, hydroxyurea, methotrexate, mycophenolate mofetil, sulfasalazine, xeljanz, 6-thioguanine, and other non-biologics.
***Prior Biologic combination therapy includes aforementioned combination of * and ** during concurrent time periods.
****Median tests have been conducted.

DISCUSSION

In line with our hypothesis, patients beginning combination therapy differed from patients on monotherapy in their medical history, demographics, and PROs. Our most salient finding was that the combination therapy group was more likely to have concomitant PsA. This is not surprising, as combinations of TNF-alpha inhibitors and agents such as MTX have been extensively studied in PsA patients relative to those with isolated dermatologic disease.[11-13] Indeed, a study from the Corrona Psoriatic Arthritis and Spondyloarthritis Registry found that a greater percentage of PsA patients were on combination therapy than monotherapy (61.3% vs 38.7%).[9] While many patients with PsA are well controlled on biologic monotherapy, these data may allow clinicians to anticipate the possible need for adjuvant systemic agents in this population and counsel patients accordingly.

Beyond this, there were no significant differences in psoriatic disease between the two groups. No discrepancies were observed in psoriasis morphology, years of psoriasis duration, or IGA, PASI, and affected BSA at treatment initiation. One might expect that patients with more widespread skin disease would be prescribed combination therapy with greater frequency, if only to elicit a rapid response before bridging to biologic monotherapy. Combinations of TNF-alpha antagonists with CsA, for instance, reduce response time substantially.[14,15] One possible explanation for these data is that newer biologic agents, such as the IL-17 antagonists (eg, ixekizumab, secukinumab), have a dramatically decreased response time when given as monotherapy.[16]

The only discrepancy in treatment history between the groups was that patients beginning combination therapy were more likely to have previously tried a non-biologic systemic agent. This could be explained by the greater percentage of combination therapy patients who have concomitant PsA, who are likely to have been prescribed non-biologic DMARDs for their rheumatologic disease in the past.

Similarly, few disparities were observed in non-dermatologic comorbid conditions. Patients on combination therapy were no more likely than monotherapy patients to report cardiovascular disease, hypertension, hyperlipidemia, diabetes mellitus, Crohn's disease, depression, or anxiety. There was a reported history of malignancy in the combination therapy group but not in the monotherapy group. However, as only one of 92 patients in the combination therapy was affected, no meaningful conclusions can be drawn about history of malignancy and the need for combination therapy. Additional information regarding the type and grade of malignancy was unavailable.

Several differences in demographics were noted between the two groups. Patients prescribed combination therapy were an average of 4.4 years older, more likely to self-identify as black, and less likely to be enrolled in commercial insurance plans. The racial disparity is unexpected, as PsA is roughly half as prevalent among Americans who identify as black versus those who identify as white (30% vs 64.5%).[17] However, the clinical significance of this is unclear.

The combination therapy group had a somewhat greater percentage of Medicare enrollees (20% vs 15%) and a significantly greater percentage of Medicaid enrollees (20% vs 7%). While it has been shown that patients with private insurance are more likely to initiate a biologic drug compared to Medicaid patients, there are currently no data on the relative ease of adding a biologic to another systemic therapy.[18]

A comparison of PROs between the two groups suggest that the need for combination therapy may be more closely related to impact on quality of life than disease severity or treatment history. Patients starting combination therapy experienced more overall fatigue, missed more hours from work, and had more problems performing activities of daily living than monotherapy patients. There was no significant difference in DLQI score; however, it has also been suggested that the DLQI survey is heavily impacted by cultural background and may not be a useful tool given the demographic differences between our groups.[19]

Key limitations of this study are its cross-sectional design and current lack of follow up data. Additionally, participating in the registry is voluntary for both providers and patients, leading to possible selection bias. Another limitation is that the majority of our patients came from the Northeast or the South, with less than a quarter of the cohort coming from the Midwest or the West. Therefore, these results may not be representative of patients on combination therapy across the country. Finally, we do not have data on what percentage of our patients came from urban, suburban, and rural environments.

CONCLUSIONS

In this study, patients on combination therapy were more likely to have concomitant PsA. These patients were also more likely to self-identify as black, more likely to report disability, and less likely to have commercial insurance. Key differences in PROs were greater reported fatigue, more missed hours from work, and more problems performing activities of daily living in the combination therapy group. These findings suggest that both medical and demographic factors contribute to a patient's likelihood to initiate combination systemic therapy for psoriasis. As more follow-up data are obtained from the Corrona Registry, future studies on longitudinal data will assess safety and efficacy of these regimens.

DISCLOSURES

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IRB statement: All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor approval and continuing review was obtained through a central institutional review board (IRB; IntegReview, Corrona-PSO-500). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRBs and documentation of approval was submitted to the sponsor before initiating any study procedures. All registry subjects were required to provide written, informed consent before participating.

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