Real-World Characteristics and Treatment Patterns of Difficult-to-Treat Psoriatic Arthritis

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Background

Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease with variable clinical presentation and treatment response. A subset of PsA patients are difficult to treat (D2T). This study compared baseline characteristics, extra-articular manifestations (EAMs), and comorbid conditions between D2T and non-difficult-to-treat (ND2T) PsA patients.

Methods

We performed a retrospective study using a de-identified federated database with 89 contributing healthcare organization including over 125 million patients. Patients with PsA (ICD-10: L40.59), ≥18 years, and at least one follow-up were included. We identified 7,403 adults with PsA treated with conventional DMARDs (Sulfasalazine, Methotrexate, Leflunomide) and recorded post-treatment CRP levels.

There is no consensus for definition of D2T PsA, but we proposed the following: prior cDMARD use, ≥2 biologic/targeted synthetic DMARDs from two different classes and elevated CRP (≥8 mg/L). Demographics, comorbidities, and EAMs were collected. We performed 1:1 propensity score matching for age, sex, race, and ethnicity. Continuous and categorical variables were analyzed using t-tests and chi-squared tests ($\alpha = 0.05$).

Results

The study included 7,403 patients (6,154 ND2T, 1,249 D2T). After propensity score matching, both groups had 1,248 patients. The D2T cohort had a higher BMI (33.1 vs. 31.7, p < 0.001) **(Table 1).**

Comorbidities, including Crohn's disease (3.2% vs. 1.9%, p = 0.045) and other psoriasis types (66% vs. 61.5%, p = 0.02), were more prevalent in the D2T group. D2T patients also had elevated CRP levels (50.4 vs. 28.4 mg/L, p < 0.001) and higher HLA-B27 positivity (2.2% vs. 0.8%, p = 0.005).

Results

	Before matching			After matching		
	Not difficult to treat N = 6,154[1]	Difficult to treat N = 1,249[1]	p-value[2]	Not difficult to treat N = 1,248[1]	Difficult to treat N = 1,248[1]	p-value[2]
Age at index	52.3 ± 13.5	47.6 ± 12.8	<0.001	47.6 ± 12.7	47.6 ± 12.8	0.931
Sex			**<0.001**			
Female	3,736 (60.7%)	852 (68.2%)		857 (68.7%)	851 (68.2%)	0.796
Race						
White	4,774 (77.6%)	1,006 (80.5%)	**0.021**	1,032 (82.7%)	1,006 (80.6%)	0.179
Black or African American	263 (4.3%)	50 (4.0%)	0.665	50 (4.0%)	50 (4.0%)	>0.999
American Indian or Alaska Native	33 (0.5%)	7 (0.6%)	0.915	3 (0.2%)	7 (0.6%)	0.205
Asian	141 (2.3%)	46 (3.7%)	**0.004**	35 (2.8%)	45 (3.6%)	0.256
Ethnicity						
Not Hispanic or Latino	4,503 (73.2%)	981 (78.5%)	**<0.001**	984 (78.8%)	980 (78.5%)	0.845
Unknown	1,166 (18.9%)	164 (13.1%)	**<0.001**	169 (13.5%)	164 (13.1%)	0.769
BMI	31.1 ± 6.7	33.1 ± 7.2	**<0.001**	31.7 ± 7.0	33.1 ± 7.2	**0.001**
Obesity (BMI > 30)	1,607 (26.1%)	354 (28.3%)	0.104	356 (28.5%)	354 (28.4%)	0.929
C-reactive protein (baseline)	14.0 ± 28.1	17.8 ± 27.5	**0.021**	14.6 ± 29.0	17.8 ± 27.5	0.148
C-reactive protein (post-cDMARDS)	28.0 ± 62.8	50.4 ± 63.4	**<0.001**	28.4 ± 59.9	50.4 ± 63.4	**<0.001**
HLA-B27 Positive	67 (1.1%)	27 (2.2%)	**0.002**	10 (0.8%)	27 (2.2%)	**0.005**
Conventional- DMARDS						
Methotrexate	4,900 (79.6%)	1,051 (84.1%)	**<0.001**	1,032 (82.7%)	1,050 (84.1%)	0.333
Sulfasalazine	1,786 (29.0%)	410 (32.8%)	**0.007**	371 (29.7%)	410 (32.9%)	0.092
Leflunomide	1,241 (20.2%)	456 (36.5%)	**<0.001**	218 (17.5%)	456 (36.5%)	**<0.001**
Comorbidities						
Hypertension	1,106 (18.0%)	188 (15.1%)	**0.013**	181 (14.5%)	188 (15.1%)	0.693
Dyslipidemia	685 (11.1%)	126 (10.1%)	0.282	103 (8.3%)	126 (10.1%)	0.111
Diabetes	1,068 (17.4%)	208 (16.7%)	0.55	197 (15.8%)	208 (16.7%)	0.55
Smoking	245 (4.0%)	60 (4.8%)	0.182	53 (4.2%)	60 (4.8%)	0.5
Chronic kidney disease	258 (4.2%)	27 (2.2%)	**<0.001**	39 (3.1%)	27 (2.2%)	0.134
Anxiety	912 (14.8%)	224 (17.9%)	**0.005**	217 (17.4%)	224 (17.9%)	0.713
Depression	665 (10.8%)	159 (12.7%)	**0.049**	147 (11.8%)	159 (12.7%)	0.464
Crohn's Disease	107 (1.7%)	40 (3.2%)	**<0.001**	24 (1.9%)	40 (3.2%)	**0.043**
Ulcerative colitis	84 (1.4%)	22 (1.8%)	0.282	13 (1.0%)	22 (1.8%)	0.126
Iridocyclitis	89 (1.4%)	19 (1.5%)	0.84	19 (1.5%)	19 (1.5%)	>0.999
Other Psoriasis	3.753 (61.0%)	824 (66.0%)	**<0.001**	768 (61.5%)	824 (66.0%)	**0.02**
Anti-TNF	2,961 (48.1%)	1,103 (88.3%)	<0.001	648 (51.9%)	1,102 (88.3%)	<0.001
Adalimumab	1,788 (29.1%)	689 (55.2%)	<0.001	409 (32.8%)	689 (55.2%)	<0.001
Certolizumab	233 (3.8%)	173 (13.9%)	<0.001	55 (4.4%)	172 (13.8%)	<0.001
Etanercept	1,277 (20.8%)	542 (43.4%)	<0.001	285 (22.8%)	542 (43.4%)	<0.001
Golimumab	275 (4.5%)	184 (14.7%)	<0.001	63 (5.0%)	184 (14.7%)	<0.001
Infliximab	653 (10.6%)	364 (29.1%)	<0.001	121 (9.7%)	364 (29.2%)	<0.001
CTLA-4	126 (2.0%)	195 (15.6%)	<0.001	24 (1.9%)	195 (15.6%)	<0.001
Abatacept	126 (2.0%)	195 (15.6%)	<0.001	24 (1.9%)	195 (15.6%)	<0.001
Anti-IL17	910 (14.8%)	1,077 (86.3%)	<0.001	197 (15.7%)	1.077 (86.3%)	<0.001
Ixekizumab	301 (4.9%)	358 (28.7%)	<0.001	73 (5.8%)	358 (28.7%)	<0.001
Secukinumab	609 (9.9%)	719 (57.6%)	<0.001	124 (9.9%)	719 (57.6%)	<0.001
Anti-IL-23	294 (4.8%)	375 (28.0%)	<0.001	73 (5.8%)	375(30.1%)	<0.001
Guselkumab	161 (2.6%)	225 (18.0%)	<0.001	45 (3.61%)	225 (18.0%)	<0.001
Risankizumab	133 (2.2%)	150 (12.0%)	<0.001	28 (2.2%)	150 (12.0%)	<0.0001
Anti-IL12/23	345 (5.6%)	454 (36.3%)	<0.001	82 (6.6%)	453 (36.3%)	<0.001
Ustekinumab	345 (5.6%)	454 (36.3%)	<0.001	82 (6.6%)	453 (36.3%)	<0.001
JAK-inhibitor	321 (5.2%)	394 (31.6%)	<0.001	73 (5.9%)	394 (31.6%)	<0.001
Tofacitinib	228 (3.7%)	283 (22.7%)	<0.001	51 (4.1%)	283 (22.7%)	<0.001
Upadacitinib	93 (1.5%)	111 (8.9%)	<0.001	22 (1.8%)	111 (8.9%)	<0.001
TYK2	3 (0.0%)	10 (0.8%)	<0.001	2 (0.2%)	10 (0.8%)	0.021
Deucravacitinib	3 (0.0%)	10 (0.8%)	<0.001	2 (0.2%)	10 (0.8%)	0.021

[1]Mean ± SD; n (%)
[2] Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

Table 1: Baseline characteristics and use of biologics and targeted synthetic DMARDs between difficult to treat and not difficult to treat psoriatic arthritis, before and after propensity score matching.

Results

The D2T group demonstrated significantly greater use of biologic and targeted synthetic DMARDs across all major therapeutic classes **(Table 1).** TNF inhibitors were used in 88.3% of D2T patients vs. 51.9% of ND2T (p < 0.001), with adalimumab most frequently prescribed (55.2% vs. 32.8%, p < 0.001).

Abatacept was also more common in D2T (15.6% vs. 1.9%, p < 0.001. IL-17 inhibitors were more frequent in D2T (86.3% vs. 15.7%, p < 0.001), primarily secukinumab (57.6% vs. 9.9%, p < 0.001). IL-23 use was higher in D2T (30.1% vs. 5.8%, p < 0.001), with guselkumab most used (18.0% vs. 3.6%, p < 0.001). IL-12/23 inhibition with ustekinumab was also more common (36.3% vs. 6.6%, p < 0.001). JAK inhibitor use was greater in D2T (31.6% vs. 5.9%, p < 0.001), mainly tofacitinib (22.7% vs. 4.1%, p < 0.001). Though rare overall, TYK2 inhibition with deucravacitinib was more common in D2T (0.8% vs. 0.2%, p = 0.021). Nearly half of the D2T group (42.4%) received four or more individual b/tsDMARDs after cDMARDs **(Table 1).**

Conclusions

Our study showed that in a matched cohort, D2T PsA patients had higher BMI, greater prevalence of Crohn's disease, additional psoriasis types, higher CRP levels, and more HLA-B27 positivity. They also had significantly higher use of biologics and targeted synthetic DMARDs across all major classes.

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