Why Do Some Psoriatic Arthritis Patients Fail Treatment? Exploring the Profile of D2T Patients

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INTRODUCTION AND OBJECTIVE

Psoriatic arthritis (PsA) is a chronic inflammatory disease combining psoriasis (Pso) and arthritis. Despite the availability of multiple therapeutic options, many patients experience residual disease activity and fail to achieve remission or low disease activity. Similar to rheumatoid arthritis, where the concept of **"difficult-to-treat"** (D2T) has emerged, studies are exploring its application to PsA.

This study aimed to compare the characteristics of D2T PsA patients with those of "good responders" (GR) to biologic disease-modifying antirheumatic drug (bDMARDs).

METHODS

A retrospective analysis of patients with PsA followed during at least two years treated with at least one bDMARD between 2010 and 2024 was conducted.

Patients were stratified into two groups (D2T-PsA vs. GR). **D2T was defined as failure to ≥1 conventional synthetic DMARD (csDMARD) and ≥2 bDMARDs**, and **GR as those who failed to ≥1 csDMARD and <2 bDMARD that used during at least two years.** Demographic, clinical, diagnostic, disease activity scores (including DAPSA, PASI) at baseline, 6 and 12 months, and therapeutic data were collected. Besides, bDMARDs number and reasons for their discontinuation were registered.

RESULTS

A total of 103 patients with PsA were included, of whom 40 (38.8%) were categorized as D2T. Clinical characteristics of both groups are shown in **Table 1**. While gender distribution was similar between groups, patients in the D2T group were significantly younger than the GR (p=0.022). Mean duration of Pso was around 28 years and PsA 17 years in both groups.

Table 1. Comparison of demographic and clinical characteristics and disease activity of GR and D2T PsA patients

Variables	GR (n=63)	D2T (n=40)	p-value
Women, n (%)	30 (47,6)	21 (52,5)	ns
Age (years), mean ± SD	**58,1 ± 12,5**	**51,4 ± 12**	**0,022**
Smoker (ever), n (%)	49 (78)	30 (75)	ns
Hypertension, n (%)	17 (28)	12 (30)	ns
Dyslipidemia, n (%)	26 (43)	17 (42,5)	ns
Diabetes, n (%)	10 (17)	5 (12,5)	ns
BMI (kg/m^2), mean ± SD	26,7 ± 3,9	27,7 ± 6	ns
PsA duration (years), mean ± SD	15,7 ± 10,5	16,9 ± 10,9	ns
Pso duration (years), mean ± SD	26,7 ± 13,5	27,8 ± 15	ns
Axial, n (%)	3 (5)	3 (8)	ns
Polyarticular, n (%)	31 (49)	18 (45)	ns
Oligoarticular, n (%)	25 (40)	18 (45)	ns
Distal interphalangeal, n (%)	26 (36)	10 (28)	ns
Enthesitis, n (%)	32 (52)	21 (52)	ns
Dactylitis, n (%)	28 (45)	14 (36)	ns
Nail involvement, n (%)	40 (68)	25 (68)	ns
RF positivity, n (%)	6 (10)	4 (10)	ns
Anti-CCP positivity, n (%)	3 (5)	0 (0)	ns
HLA-B27 positivity, n (%)	4 (7)	4 (11)	ns
Fibromyalgia, n (%)	**5 (8)**	**12 (30)**	**0,006**
DAPSA before, mean ± SD	28,6 ± 12,6	30,8 ± 9,7	ns
DAPSA at 6m, mean ± SD	**11,1 ± 8,9**	**17,9 ± 8,4**	**0,010**
DAPSA at 12m, mean ± SD	**7,3 ± 5,4**	**17,5 ± 14**	**0,048**
PASI before, mean ± SD	**9,5 ± 5,9**	**15,6 ± 8,4**	**0,017**
PASI at 6m, mean ± SD	3,2 ± 4,1	3,3 ± 3,8	ns
PASI at 12m, mean ± SD	1 ± 1,4	1,4 ± 2,2	ns
CPR (mg/L) before, mean ± SD	8,9 ± 11,5	7,5 ± 7,0	ns
CPR (mg/L) at 6m, mean ± SD	5,1 ± 6,8	3,7 ± 6,2	ns
CPR (mg/L) at 12m, mean ± SD	2,8 ± 3,0	6,0 ± 8,4	ns

Cardiovascular risk factors did not differ between groups. Nonetheless, fibromyalgia (FM) was more prevalent in the D2T group (p=0.006). No differences were observed in musculoskeletal manifestations, nail involvement, or serological features, including HLA-B27 positivity. Regarding disease activity, baseline DAPSA scores were similar between groups, while at 6 and 12 months post-bDMARD initiation, DAPSA scores were significantly higher in the D2T group. Baseline PASI scores were higher in the D2T group, although differences were not observed at 6 and 12 months.

Tumour necrosis factor inhibitors were the most used bDMARDs in both groups. As seen in **Figure 1**, the most frequent reason for discontinuation was the primary inefficacy (52%) in the group of GR, while in the D2T group secondary inefficacy (40%) was the most frequent cause.

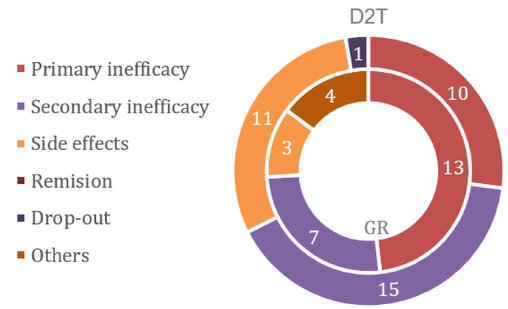

Figure 1: Cause of discontinuation of the first bDMARD of GR and D2T.

CONCLUSIONS

Around one third of PsA patients requiring bDMARDs met D2T criteria. **This subset was characterised by younger patients with higher disease activity, greater severity of Pso, and a higher prevalence of FM, while we found no differences in baseline activity by DAPSA or other variables.** Further studies are needed to identify predictors of refractory disease in order to improve management.

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