Characteristics of Patients with Psoriasis with Psoriasis Area and Severity Index < 10 Treated with Biological Agents: Results from the French PsoBioTeq Cohort

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Dear Editor,

The decision to initiate systemic therapy in psoriasis is based mainly on disease severity assessments, determined using physicians-derived scores. A commonly used assessment is the Psoriasis Area and Severity Index (PASI), with an absolute value of 10 or more indicating severe disease.[1] How patients perceive the severity of psoriasis and physicians' evaluations may be discordant, especially when lesions involve visible areas or are associated with itching. Such lesions can have a greater impact on quality of life (QoL),[2] as evaluated using patient-reported outcomes such as the Dermatology Life Quality Index (DLQI). Analysis of the Swedish PsoReg registry found that patients with high PASI and low DLQI were more likely to receive biologics than those with low PASI and high DLQI.[3] A retrospective study of 54 patients showed that DLQI guides therapeutic decisions in patients with PASI ≤6, with improvement of both disease and QoL scores following systemic therapy.[4] A recent international Delphi consensus challenged the severity criteria,[5] and guidelines[1,6] propose considering systemic therapy when psoriasis involves impactful areas or is recalcitrant to topical therapy, whatever the PASI.

To understand better the determinants of clinical decisions other that disease severity, we aimed to describe the clinical profiles and main outcomes of patients with PASI <10 for whom biologics were initiated in the real-life French PsoBioTeq cohort.[7] The PsoBioTeq study was approved by the 'Comite d'Evaluation de l'Ethique des Projets de Recherche Biomedicale du GHU Nord' (JMD/MDM/177-11) and was registered on Clinical Trials.gov (NCT01617018).

Between July 2012 to July 2016, 1027 patients initiated biologics and had available PASI data at inclusion. We compared patients with PASI <10 vs. ≥10 for baseline variables (socio-

demographic data, choice of biologic, type and location of psoriasis, PASI and DLQI), treatment response and drug survival. Descriptive analysis used n (%), mean (SD) and survival curves with the Kaplan-Meier method. Groups were compared using the chi-squared, Fisher, Student's t or log-rank test, as appropriate.

Table 1 presents the characteristics of the 1027 patients. Among them, 403 (39.2%) had PASI <10. We found no difference between groups for age and socioprofessional categories. Women more frequently had PASI <10 (43.4% vs. 32.2%, $p < 0.001$). Body mass index also differed, with obese patients less often having PASI <10 (25.3% vs. 34.6%, $p=0.01$). In the whole cohort, 91.4% of patients presented plaque-type psoriasis, without any difference between PASI groups. Psoriasis restricted to visible areas (face, palms, nails, folds) was most frequent in the PASI <10 group (5.0% vs. 1.2%, $p<0.001$). DLQI >10 was more frequent in the PASI ≥10 group (52.0% vs. 33.8%). However, 52.7% of the 256 patients with a very low PASI (0-6) had DLQI > 10.

Before initiating biologics, 90.7% of all study patients received at least one systemic conventional treatment. The two most frequently prescribed first-line biologics in the cohort were adalimumab and ustekinumab, with a different distribution between the 2 groups (adalimumab 36.0% vs. 45.7%; ustekinumab 32.8% vs. 27.2% in PASI <10 and ≥10 groups, respectively).

Biologic drug survival did not differ significantly across the two PASI groups: median survival 23.2 months (range 19.3-27.9) in the PASI <10 group and median 27 months (range 23.1-31.8) in the PASI ≥10 group ($p=0.23$). Time to achieve ≥ 75% reduction of baseline PASI was significantly delayed in the PASI <10 group: median time of 12.2 months (range 10.2-14.0) vs 6.7 months (range 6.3-7.1); $p<0.001$. Time to achieve a DLQI of 0 or 1 did not statistically differ between the two groups ($p=0.13$).

In conclusion, we found that 39% of patients in the PsoBioTeq cohort in whom biologics were initiated had PASI <10 at initiation. This was not the consequence of a high frequency of non-plaque-type psoriasis, such as palmo-plantar pustulosis, for which PASI is not appropriate. The main differences between patients from the two groups were that patients with PASI <10 were more frequently women and not obese and had higher-frequency involvement of impactful areas. Such localisations have a known impact on social well-being.[2] One third of these patients reported a significant impact on QoL (DLQI >10), and this reached 52.7% in the low-PASI (0-6) subgroup. These characteristics might explain the decision to start biologics in some of these patients, even if the PASI score was low. Therapeutic maintenance was favorable in the PASI<10 group, although no formal comparison can be made with the PASI > 10 group due to differences in therapeutic regimen between the two groups.

Altogether, this study is in accordance with increasing evidence that, in addition to PASI, the decision to initiate biologics considers patient-specific treatment goals, especially for impactful skin sites, with lack of disease control under conventional treatments.[5,6,8] More data are needed to address the needs of patients with limited disease severity and high impact of psoriasis on QoL to plan for appropriate therapeutic intervention.

References

1. Amatore F, Villani AP, Tauber M, Viguier M, Guillot B; Psoriasis Research Group of the French Society of Dermatology French guidelines on the use of systemic treatments for moderate-to-severe psoriasis in adults. J Eur Acad Dermatol Venereol. 2019;33:464-483.
2. Lebwohl MG, Bachelez H, Barker J et al. Patient perspectives in the management of psoriasis. Results from the population-based multinational assessment of psoriasis and psoriasis arthritis survey. *J Am Acad Dermatol 2014;* 70:871-81.
3. Hagg D, Sundstrom A, Eriksson M et al. Decision for biological treatment in real life is more strongly associated with the PASI that with the DLQI. *J Eur Acad Dermatol Venereol* 2015:29: 452-6

4. Mermin D, Boursault L, Milpied B, Taieb A, Ezzedine K, Seneschal J. DLQI as a major criterion for introduction of systemic agents in patients with mild psoriasis. *J Eur Acad Dermatol Venereol.* 2016;30:1961-1964.
5. Strober B, Ryan C, van de Kerkhof P et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. *J Am Acad Dermatol.* 2020;82:117-122.
6. Nast A, Smith C, Spuls PI, et al. EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris - Part 1: treatment and monitoring recommendations *J Eur Acad Dermatol Venereol.* 2020;34:2461-2498.
7. Sbidian E, Giboin C, Bachelez H et al. Factors associated with the choice of the first biologic in psoriasis: real-life analysis from the Psobioteq cohort. *J Eur Acad Dermatol Venereol.* 2017;31:2046-2054.
8. Bergqvist C, Stern RS, Chosidow O. Psoriasis: an example of the complexity of decision-making. *Br J Dermatol.* 2020 Dec 10. doi: 10.1111/bjd.19715.

Table 1: Characteristics of the 1027 patients who initiated biologics and had reported baseline Psoriasis Area and Severity Index (PASI)

	PASI <10 (n=403)	PASI ≥10 (n=624)	Total (n=1027)	p-value
Main psoriasis data: n (%)				
Plaques	357 (90.8%)	548 (91.8%)	905 (91.4%)	0.60
Other forms	36 (9.2%)	49 (8.2%)	85 (8.6%)	
Missing	10	27	37	
Restricted to impactful areas	19 (5%)	7 (1.2%)	26 (2.7%)	0.0005
Missing	20	46	66	
DLQI >10	134 (33.8%)	318 (52%)	452 (44.8%)	<0.0001
Missing	6	12	18	
Socio-demographic data				
Age (year)				0.45
Median age	45	46	46	
Range	19; 83	18; 84	18; 84	
Female: n (%)	175 (43.4%)	201 (32.2%)	376 (36.6%)	0.0003
BMI: n (%)				0.012
<25	137 (38.5%)	187 (34.2%)	324 (35.9%)	
25-30	129 (36.2%)	170 (31.1%)	299 (33.1%)	
> 30	90 (25.3%)	189 (34.6%)	279 (30.9%)	
Missing	47	78	125	
Therapeutic interventions received before biologic initiation				
Topical	377 (97.4%)	566 (97.3%)	943 (97.3%)	
UVB-therapy	113 (30.4%)	195 (35.5%)	308 (33.4%)	
PUVA-therapy	197 (52.5%)	324 (57.3%)	521 (55.4%)	
Conventional systemic(s)*	376 (93.3%)	555 (89%)	931 (90.7%)	
First biologic at inclusion: n (%)				0.006
Etanercept	113 (28%)	140 (22.4%)	253 (24.6%)	
Infliximab	13 (3.2%)	29 (4.6%)	42 (4.1%)	
Adalimumab	145 (36%)	285 (45.7%)	430 (41.9%)	
Ustekinumab	132 (32.8%)	170 (27.2%)	302 (29.4%)	
Biologic drug survival, in months: median [range]	23.2 [19.3-27.9]	27 [23.1-31.8]		0.23
Time to achieve PASI75, in months: median [range]	12.2 [10.2-14.0]	6.7 [6.3-7.1])		0.0001
Time to achieve DLQI(0/1), in months: median [range]**	61.6 [13.3-61.6]	15.0 [9.5-28.29]		0.13

** at least one conventional systemic therapy*

*** in the patients with baseline DLQI >1 (335 for PASI <10 group and 556 for PASI ≥10 group)*