

# Predictors of biologic treatment of psoriasis: a non-interventional study

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**Background:** Biologic therapies represent a significant advance in the treatment of psoriasis. However, no studies have examined the patient characteristics predictive of biologic treatment of psoriasis. The purpose of this study was to ascertain the frequency and predictors of treatment of psoriasis with biologics in three European countries, ie, France, Spain, and the UK.

**Methods:** This was a cross-sectional analysis of physician-recorded demographic and clinical data on patients receiving either conventional or biologic treatments for psoriasis. Data were drawn from the Adelphi 2007 Psoriasis Disease Specific Program (DSP®), a multinational, real-world survey of patients with psoriasis consulting practicing dermatologists. The numbers of patients treated with biologic and nonbiologic agents were recorded. Data were subjected to bivariate analysis according to treatment regimen (biologic versus nonbiologic). Predictors of treatment with biologics were identified by logistic regression analysis.

**Results:** A total of 2,509 psoriasis patients were included in this study (1,374 from France, 561 from Spain, and 574 from the UK). Biologic use was most prevalent in Spain (19.4% of patients), followed by the UK (9.1%), and France (8.4%). In the logistic regression analysis, psoriatic arthritis was a statistically significant predictor of increased biologic use in France (odds ratio [OR] 5.38, 95% confidence interval [CI] 3.32–8.77), Spain (OR 2.71, 95% CI 1.16–6.33), and the UK (OR 8.70, 95% CI 3.65–20.83). Physician-assessed moderate-to-severe disease was also a statistically significant predictor of increased biologic use in France (OR 5.08, 95% CI 2.01–12.82), Spain (OR 11.11, 95% CI 4.33–28.57), and the UK (OR 8.55, 95% CI 1.11–66.67).

**Conclusion:** In this study, an average of about one tenth of psoriasis patients enrolled in Spain, France, and the UK were treated with biologics in 2007. Physician-assessed moderate-to-severe disease and presence of psoriatic arthritis were significantly associated with biologic use in all three countries.

**Keywords:** psoriasis, drug therapy, tumor necrosis factor-alpha, antagonists, inhibitors, dermatologic agents, therapeutic use

## Introduction

Psoriasis is a chronic, genetically based, and immune-mediated inflammatory disorder affecting 2%–3% of the Caucasian population in western countries.<sup>1</sup> These plaques may be localized or widespread across the body.<sup>2</sup> The fingernails and toenails are involved in 40% of psoriasis cases, with thickening and/or pitting of the nails as common manifestations.<sup>3–5</sup>

The chronic inflammation underlying psoriasis affects the joints as psoriatic arthritis. The prevalence of psoriatic arthritis among patients with plaque psoriasis

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ranged from 5.9% to 23.9% (median 11.2%) in eight US and European studies using rheumatologically validated criteria.<sup>6</sup> Cardiovascular risk factors such as obesity, metabolic syndrome, and hypertension are frequent comorbidities of psoriasis,<sup>7–10</sup> possibly due to common inflammatory pathways.<sup>11</sup>

In limited (mild) disease, the most commonly used therapy is topical with the addition of phototherapy in refractory cases. In moderate-to-severe psoriasis, phototherapy alone combined with systemic therapy or systemic therapy alone is recommended. Recent guidelines present the level of evidence for the efficacy of the available therapies and give recommendations for their use in daily practice.<sup>12</sup>

Significant advances have been made in the treatment of psoriasis with the availability of biologic therapies. Biologics approved for the treatment of psoriasis in Europe are the tumor necrosis factor- $\alpha$  antagonists, ie, infliximab, etanercept, and adalimumab, and the anti-p40 agent, ustekinumab.<sup>2</sup>

European and UK guidelines recommend biologics only for patients with moderate-to-severe psoriasis who have not responded to or are intolerant of conventional therapies.<sup>13–17</sup> In a recent European consensus, moderate-to-severe psoriasis was defined as a body surface area  $>10$  or psoriasis area and severity index (PASI)  $>10$  and dermatology life quality index (DLQI)  $>10$ .<sup>18</sup> The British Association of Dermatologists recommends biologics only for patients who have severe psoriasis, defined as a PASI score  $\geq 10$  and a DLQI score  $>10$ .<sup>18</sup> These criteria are less stringent than those of the UK National Institute for Health and Clinical Excellence for use of infliximab in psoriasis, which recommend infliximab only for very severe psoriasis, defined as a PASI score  $\geq 20$  and a DLQI score  $>18$ .<sup>19</sup>

These guidelines provide insight into which patients are eligible for treatment with biologics, but there is little information in the literature about the determinants of treatment of psoriasis with biologics in clinical practice. This study was designed to examine variables associated with biologic treatment in populations of psoriasis patients from France, Spain, and the UK.

## Materials and methods

### Study design

This was a cross-sectional analysis of physician-recorded demographic and clinical data on patients receiving treatment for psoriasis. Data were drawn from the Adelpi 2007 Psoriasis Disease Specific Program (DSP<sup>®</sup>), a multinational, real-world survey of patients with psoriasis

consulting practicing dermatologists. Physicians were identified from the public lists of health care professionals and were screened for eligibility based on the criteria of whether they were licensed physicians between 1970 and 2006, specialized in dermatology, and actively managing ten or more psoriasis patients per month. Each physician was asked to recruit 8–10 consecutive patients presenting with psoriasis in his/her office. One hundred and forty-three physicians were recruited from France and 61 physicians were recruited from both Spain and the UK ( $n=265$ ) to complete a detailed patient record form for patients presenting with psoriasis and receiving a prescription for topical agents, phototherapy, or systemic treatment during routine visits in the calendar year 2007. Patients who were 18 years or older and diagnosed as having psoriasis were recruited. Patients who had a missing value for age or gender were excluded from the data analysis.

### Variables

The patient record form included demographics, body mass index, disease symptoms and severity determined by PASI scores, current and previous treatments, patient-reported disease management strategies, the physician's assessment of current severity and severity at diagnosis, the patient's PASI score, and physician-reported reasons for clinical decisions and prescribing. PASI scores were based on the extent of psoriasis in four specific body surface areas (head, trunk, upper limbs, and lower limbs) and the degree of plaque erythema (redness), scaling, and thickness as described by Fredriksson and Pettersson.<sup>20</sup> The numeric PASI score ranges from 0 (absence of disease) to 72 (maximal disease). The severity of disease was determined from the PASI scores, and the proportions of patients with mild (PASI score  $<10$ ) and moderate-to-severe (PASI score  $\geq 10$ ) disease. Obesity was defined as a body mass index  $\geq 30$ . Nonbiologic treatments in this study included topical (eg, corticosteroids, vitamin D3), phototherapy (eg, natural sunlight or ultraviolet A or B irradiation), and traditional systemic (eg, methotrexate, cyclosporine). Biologics in this study included infliximab, etanercept, adalimumab, and efalizumab.

### Statistical analysis

Patient characteristics were analyzed descriptively for the total study samples from each country and then assessed in a bivariate analysis according to treatment with biologics (yes or no). The statistical significance of the distributions across treatment was determined by Student's *t*-test for continuous data (age and PASI score) and by chi-square or Fisher's Exact



one quarter of patients in France (25.8%) and Spain (29.4%) had nail involvement, but the percentage was numerically higher in the UK (42.5%). In our bivariate assessment of patient characteristics associated with biologic use, psoriatic arthritis was significantly associated with biologic use in all three countries. Obesity, PASI score, and nail involvement were also found to be significantly associated with biologic use in patients from France and Spain.

## Patient characteristics associated with biologic use

Use of biologics was reported in 11.2% (n=282) of the total patient population (Table 2). Biologic use was most prevalent in Spain (19.4%), followed by France (9.1%) and the UK (8.4%). Among patients with physician-assessed mild disease, biologic use was 8.2% in France, 12.8% in Spain, and 7.1% in the UK (Table 3). Among patients with physician-assessed moderate-to-severe psoriasis, biologic use was 27.8% in Spain, followed by France (9.7%) and the UK (9.3%). Physician-assessed moderate-to-severe disease was also significantly associated with biologic use in all three countries (all comparisons  $P < 0.0005$ ).

## Distribution of psoriasis severity and correlation with PASI score

The distribution of physician-assessed psoriasis severity varied significantly between countries ( $P < 0.001$ , Table 4). There were more patients with mild disease than moderate disease and severe disease in Spain (55.6%, 37.6%, and 6.6%, respectively) and the UK (43.9%, 39.4%, and 16.7%, respectively). There were more patients with moderate disease than mild disease and severe disease in France (44.8%, 40.6%, and 14.6%, respectively). Physician-assessed psoriasis severity correlated strongly with PASI scores in each country (Spearman coefficient  $R = 0.699$ , Table 5).

## Predictors of biologic use

In the logistic regression analysis (Table 6), psoriatic arthritis was a statistically significant predictor of increased biologic

use in France (odds ratio [OR] 5.38, 95% confidence interval [CI] 3.32–8.77), Spain (OR 2.71, 95% CI 1.16–6.33), and the UK (OR 8.70, 95% CI 3.65–20.83). Consistent with this is our finding that patients with psoriatic arthritis had a greater prevalence of PASI score-based moderate-to-severe disease as compared with those patients with psoriasis only (Figure 1).

Physician-assessed moderate-to-severe disease was also a statistically significant predictor of increased biologic use in France (OR 5.08, 95% CI 2.01–12.82), Spain (OR 11.11, 95% CI 4.33–28.57), and the UK (OR 8.55, 95% CI 1.11–66.67).

No other variables were consistent across countries, although higher PASI scores increased the odds of using biologics in France (OR 1.05, 95% CI 1.02–1.08) and Spain (OR 1.02, 95% CI 1.00–1.05). Obesity was found to be associated with increased odds of biologic use only in France (OR 2.29, 95% CI 1.33–3.95).

## Discussion

In this study, an average of about one tenth of psoriasis patients enrolled in Spain, France, and the UK were treated with biologics in 2007. The European Medicines Agency requires that only those patients with moderate-to-severe psoriasis and an inadequate response to conventional systemic medications (or adverse effects/contraindication to these agents) are eligible for prescription of biologics in the European Union.<sup>13–16</sup> The primary caveat to the assessment of patient eligibility for biologic treatment in this study is the lack of information in the Adelphi database on patient history regarding response to conventional therapies. Although a determination of moderate-to-severe disease implies prior therapies had been ineffective, the proportion of patients who had failed to respond to conventional therapies was unknown, and therefore the true percentage of eligible patients cannot be determined. However, the mean PASI score was found to be significantly higher among patients on biologic treatment than in those with nonbiologic treatment in France ( $P < 0.0001$ ) and in Spain

**Table 2** Patient treatment by country

	All patients (n=2,509)	France (n=1,374)	Spain (n=561)	UK (n=574)
Biologic treatment	282 (11.2%)	125 (9.1%)	109 (19.4%)	48 (8.4%)
Nonbiologic treatment	2,227 (88.8%)	1,249 (90.9%)	452 (80.6%)	526 (91.6%)
Topical	1,257 (50.1%)	777 (56.6%)	295 (52.6%)	185 (32.2%)
Phototherapy	276 (11.0%)	182 (13.2%)	31 (5.5%)	63 (11.0%)
Traditional systemic	694 (27.7%)	290 (21.1%)	126 (22.5%)	278 (48.4%)





**Table 6** Predictors of current biologic treatment

	Adjusted odds ratio (95% CI) <sup>a</sup>					
	France (n=1,266)		Spain (n=466)		UK (n=333)	
Increasing age	1.00	(0.99–1.02)	0.99	(0.97–1.00)	0.99	(0.96–1.01)
Female	0.94	(0.62–1.54)	0.79	(0.47–1.32)	1.19	(0.55–2.57)
BMI ≥30 versus BMI <30	<b>2.29</b>	<b>(1.33–3.95)</b>	1.38	(0.62–3.13)	1.81	(0.80–4.11)
Nail involvement	1.49	(0.96–2.32)	1.30	(0.76–2.25)	0.90	(0.40–2.00)
Increasing PASI score	<b>1.05</b>	<b>(1.02–1.08)</b>	1.02	(1.00–1.05)	1.00	(0.95–1.05)
Moderate-to-severe disease <sup>b</sup>	<b>5.08</b>	<b>(2.01–12.82)</b>	<b>11.11</b>	<b>(4.33–28.57)</b>	<b>8.55</b>	<b>(1.11–66.67)</b>
Psoriatic arthritis	<b>5.38</b>	<b>(3.32–8.77)</b>	<b>2.71</b>	<b>(1.16–6.33)</b>	<b>8.70</b>	<b>(3.65–20.83)</b>

**Notes:** <sup>a</sup>Bold text indicates statistical significance; <sup>b</sup>physician-assessed disease severity, moderate and severe patients are combined.

**Abbreviations:** BMI, body mass index; CI, confidence interval; PASI, Psoriasis Area and Severity Index.

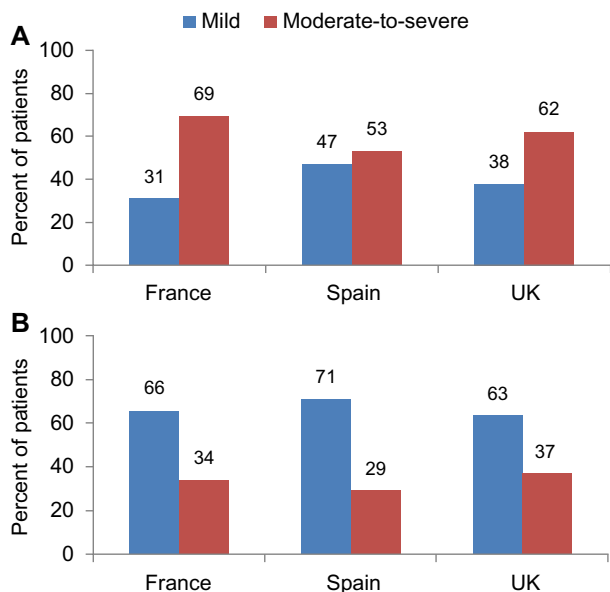
a subjective assessment of physician severity, which was done by dermatologists presumably familiar with the diagnosis and management of psoriasis, was found to be a significant predictor, and not PASI score, which is an objective measure. A physician's severity assessment may be driving the treatment decision to prescribe biologics rather than an objective measure in clinical practice. However, the lack of association might speak to the imputation method used to calculate PASI score for those patients where it was missing.

The PASI index does not specifically include nail psoriasis or the presence of psoriatic arthritis, which may reflect greater disease severity. Although these other variables

related to disease severity were negatively associated with biologic treatment in the bivariate analyses, psoriatic arthritis was predictive of treatment with biologics in the regression model (statistically significant for Spain, numerically so for France), consistent with the greater disease severity observed in patients with psoriatic arthritis. According to Spanish guidelines, the presence of arthritis is a criterion for prescription of biologics.<sup>26</sup> Because of the cross-sectional design of this study, we could not tell whether biologic use was the reason for lower PASI scores. We must speculate that the effectiveness of biologic therapy was at least part of the reason for the negative association.

To date there are no reliable predictors of response to tumor necrosis factor-alpha antagonists as a class (regardless of disease),<sup>27</sup> and few studies have been performed to identify genetic predictors of response to biologics in psoriasis.<sup>28</sup> Studies of variables associated with the clinical response of psoriatic arthritis to tumor necrosis factor-alpha antagonists have identified younger age<sup>29,30</sup> and male sex.<sup>29,31</sup> In the present study, both age and female sex were not predictive of treatment with biologics.

Several limitations in this analysis stem from the data source. The data set refers to treatment patterns in 2007, which do not necessarily reflect current trends in biologic use. The proportions of patients seen in this study are not representative of psoriasis patients in general. The majority of mild-moderate patients are seen primarily by primary care practices. Further, as noted above, there was no documentation of prior failure to respond to conventional therapies. Data on PASI scores were not available for all patients. The paucity of PASI scores in the database required imputation of scores for most of the study population. As stated in the Materials and methods section, the correlation between actual and predicted PASI scores was moderate ( $R=0.51$ ). In addition, we observed no difference between



**Figure 1** Distribution of psoriasis severity\* in patients with (A) psoriatic arthritis and (B) psoriasis only.

**Notes:** \*Severity was determined by PASI scores as described in the Materials and methods section. Distribution of mild versus moderate-to-severe disease was significantly different in patients with psoriatic arthritis than those with psoriasis only ( $P \leq 0.004$  for each country in chi-square tests).  $n=1,269$  for France, 551 for Spain, and 507 for the UK.

**Abbreviation:** PASI, Psoriasis Area and Severity Index.

actual and imputed mean PASI scores for patients treated with biologics versus patients treated with nonbiologics (including topicals only, phototherapy, and conventional systemic therapy).

In conclusion, an average of about one tenth of the psoriasis patients enrolled in this study in Spain, France, and the UK were treated with biologics. Physician-assessed moderate-to-severe disease and the presence of psoriatic arthritis were significantly predictive of biologic use in all three countries.

## Disclosure

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