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Letter

Axial Spondyloarthritis Disease Activity Cutoffs at Golimumab Initiation in the French GO-PRACTICE Study: Parallels With the German GO-NICE Study

To the Editor:

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disorder that includes both radiographic and nonradiographic entities[1]. International guidelines for axSpA management recommend nonsteroidal antiinflammatory drugs as the first line of treatment[2,3]. Initiation of anti-tumor necrosis factor-α (anti-TNF-α) therapy is recommended in patients with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[4] of 4.0 and above, the cutoff signifying active disease[2,5]. Additionally, the influence of elevated baseline C-reactive protein (CRP) on major clinical response to anti-TNF-α treatment in ankylosing spondylitis (AS) has been demonstrated[6] and the existing French guidelines for axSpA management do not recommend biologics for nonradiographic axSpA unless signs of inflammation are confirmed by magnetic resonance imaging or elevated CRP[7].

In the German GO-NICE study, the effectiveness of the anti-TNF-α golimumab (GOL) was assessed in 501 patients with AS over 2 years, using the BASDAI[8]. A posthoc analysis of 244 biologic-naïve patients with AS revealed that even those with baseline BASDAI as low as 2.8 responded significantly to GOL. Baseline CRP, however, had no effect on disease activity improvement[9]. Our objective is to supplement these findings by presenting a similar posthoc analysis from the French GO-PRACTICE study, the results of which provide further evidence to challenge the current BASDAI cutoff of 4.0 for anti-TNF-α initiation.

GO-PRACTICE was a prospective, observational study performed in real-life settings in France. Its main objective was to evaluate the persistence of GOL treatment at 2 years. Patients with axSpA, rheumatoid arthritis, and psoriatic arthritis were consecutively included upon GOL initiation between January 2015 and March 2016, and were observed from baseline up to 2 years, with in-clinic visits every 12 months. BASDAI questionnaires were answered by patients with axSpA every 3 months until GOL discontinuation or study end.

The GO-PRACTICE study was approved by the French National Ethics Committee (CCTIRS) on June 12, 2014 (Dossier no. 14.412). At the time of enrollment, patients were informed prior to giving their consent that the results of this study may eventually be published. However, no special written informed consent was taken from patients prior to publishing this article, as the data do not disclose any sensitive or personal information and are completely anonymous. The study was registered in the EU PAS Register (EUPAS7527).

Of 478 patients with axSpA, 291 (60.9%) were biologic-naïve. Baseline BASDAI was unavailable for 30 patients. Our analysis population thus consisted of 261 patients with axSpA subdivided into 3 groups (Appendix 1): the majority with baseline BASDAI ≥ 4.0 (group 1: n = 209, 80.0%), those with baseline BASDAI ≥ 2.8 to < 4.0 (group 2: n = 30, 11.5%), and baseline BASDAI < 2.8 (group 3: n = 22, 8.4%). Patients in group 1 and group 2 were further divided in 2 subgroups, those with elevated baseline serum CRP (≥ 5 mg/L; group 1: n = 115, and group 2: n = 15) and those with non-elevated CRP (group 1: n = 89, group 2: n = 15). Baseline CRP data were missing for 5 patients in group 1.

Most baseline characteristics were similar among the 3 groups (Appendix 1). Mean age was 39.9 ± 11.0 years and 50.2% were males. Median duration since axSpA diagnosis was 1.7 years (range 0–45.1) and 56.6% of the analyzable population had elevated serum CRP.

Figure 1 depicts the evolution of mean BASDAI for each group. Disease activity improvement at 2 years was significant across all 3 groups for those persisting on GOL, but was clinically important in group 1 and group 2 (the minimum clinically important improvement cutoff for BASDAI is 1.1 points[10]), thus signifying a positive response to GOL. This response was strongest in group 1 patients, for whom baseline BASDAI decreased by a mean of 3.2 points over 2 years, compared to a decrease of 1.2 in group 2 and 0.7 points in group 3, respectively (all $P < 0.0001$ vs baseline). This evolution, however, should be interpreted cautiously for the latter 2 groups, owing to higher intertrimestral fluctuations in disease activity, which could partly be explained by the smaller patient numbers.

Baseline CRP appeared to have an effect on BASDAI improvement over 2 years for group 1 (Figure 2A). Those with elevated baseline CRP showed a significantly higher treatment response compared to patients with normal CRP values, despite similar baseline BASDAI values. Mean baseline and 2-year BASDAI scores for group 2 patients with normal and elevated CRP are similar (Figure 2B); nevertheless, those with elevated CRP seemed to show greater BASDAI improvement in the early months of treatment.

Among biologic-naïve axSpA patients who were prescribed GOL in the GO-PRACTICE study, 20.0% had baseline BASDAI below the recommended threshold of 4.0 for anti-TNF-α initiation, a lower proportion than observed in GO-NICE (29.5%). A clinically important improvement in BASDAI was observed at 2 years for group 1 and group 2 patients persisting on GOL. Whereas baseline CRP levels did not seem to influence patient response in GO-NICE, those with elevated baseline CRP in group 1 (baseline BASDAI ≥ 4.0) in the GO-PRACTICE study demonstrated greater benefit from GOL than those with normal CRP. Our findings lead us to support the conclusion made by Braun, *et al*[9] that the recognized BASDAI cutoff of 4.0 for anti-TNF-α initiation should be reevaluated and lowered. We additionally concur that elevated CRP be taken into consideration as part of the physicians' decision to initiate anti-TNF-α treatment in axSpA.

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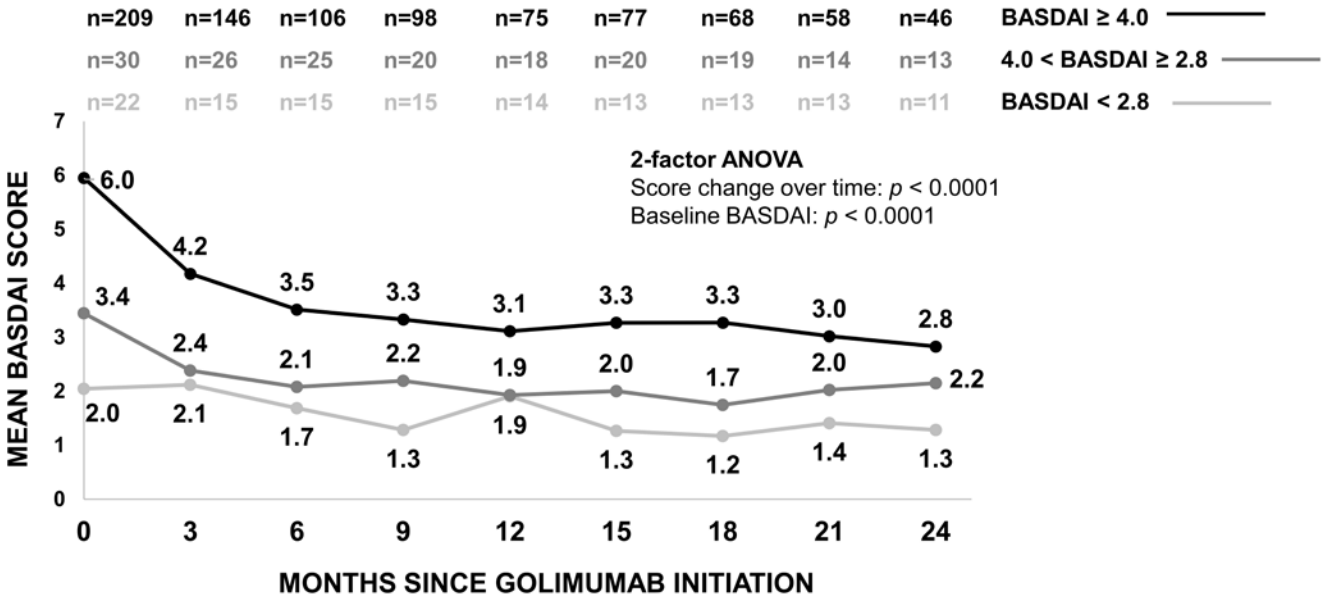

Figure 1. Evolution of BASDAI scores over 2 years based on baseline disease activity index. The evolution of BASDAI scores from baseline and every 3 months up to 2 years is shown for biologic-naïve axSpA patients who were divided into 3 subgroups based on baseline BASDAI of ≥ 4.0 (black), ≥ 2.8 and < 4.0 (dark grey), and < 2.8 (light grey). *P* is determined from a 2-factor repeated measures method comparing the 3 subgroups. AxSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

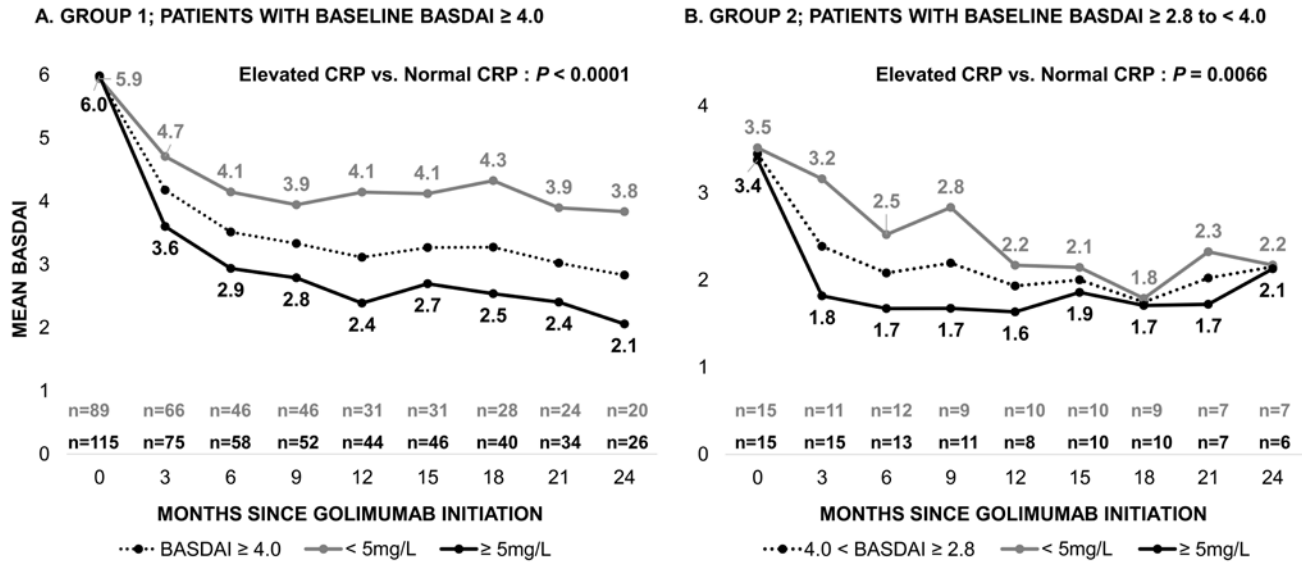

Figure 2. BASDAI evolution in biologic-naïve axSpA patients with (A) baseline BASDAI ≥ 4.0 (group 1), and (B) 2.8 ≤ BASDAI < 4.0 (group 2), in relation to baseline serum CRP levels. Patients were subdivided into 2 groups based on serum CRP levels: ≥ 5 mg/L (elevated CRP) and < 5 mg/L (normal CRP). *P* is determined from a repeated measures method comparing the normal CRP and elevated CRP subgroups. AxSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein.

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APPENDIX 1. Baseline characteristics of biologics-naïve patients with axSpA according to 3 categories of BASDAI scores at baseline.

	BASDAI at Baseline (GOL Initiation)				
	Group 1, n = 209	Group 2, n = 30	Group 3, n = 22	Total, n = 261	*P*
Age, yrs	n = 209	n = 30	n = 22	n = 261	NS
Mean (SD)	40.0 (10.7)	40.8 (13.0)	37.2 (10.9)	39.9 (11.0)	
Median	39	39	36	39	
Range	19–71	24–69	25–62	19–71	
Male, n (%)	94 (45.0)	20 (66.7)	17 (77.3)	131 (50.2)	**0.002**
Time elapsed since diagnosis, yrs	n = 200	n = 28	n = 21	n = 249	NS
Mean (SD)	5.2 (7.4)	7.7 (10.4)	3.8 (5.9)	5.3 (7.7)	
Median	1.70	3.13	1.19	1.71	
Range	0.02–45.10	0.10–37.65	0.15–22.45	0.02–45.10	
CRP, mg/L	n = 204	n = 30	n = 22	n = 256	NS
Mean (SD)	11.8 (18.4)	13.3 (19.0)	15.3 (20.2)	12.3 (18.6)	
Median	5.45	4.75	5.55	5.35	
Range	0.1–137	0.7–73	1–70	0.1–137	
CRP ≥ 5 mg/L, n (%)	n = 204	n = 30	n = 22	n = 256	NS
No	89 (43.6)	15 (50.0)	7 (31.8)	111 (43.4)	
Yes	115 (56.4)	15 (50.0)	15 (68.2)	145 (56.6)	

Values in bold face are statistically significant. The significance level has been defined at $P < 0.05$. Patients in group 1 had baseline BASDAI of ≥ 4.0. Those in group 2 had baseline BASDAI < 4.0 and ≥ 2.8 and in group 3 < 2.8. AxSpa: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; GOL: golimumab; NS: not significant.