Secukinumab efficacy in patients with PsA is not dependent on patients' body mass index

We read with interest the recently published paper from McGonagle *et al*[1] analysing the role of interleukin (IL)-17A in axial spondyloarthritis and psoriatic arthritis (PsA). The meta-analysis and functional study provided by the authors highlighted the efficacy of IL-17A block by secukinumab in the treatment of PsA. However, there is no mention of the role of body mass index (BMI), if any, in influencing the clinical response to secukinumab, given the lack of published data. PsA is a chronic inflammatory arthritis burdened by a series of metabolic comorbidities. Among them, obesity is very common in PsA, with a prevalence of 27%, as confirmed by a recent Spanish work.[2] Obesity in PsA has been associated with higher disease activity and a worse effectiveness of biologic treatment in PsA. This has been certainly proven for anti-tumour necrosis factor (TNF)-α as demonstrated by different studies reporting, in obese patients, a reduced treatment response and adherence. In particular, results coming from DAN-BIO and ICE-BIO registries[3] point out that obesity is a risk factor for anti-TNF withdrawal due to poor response. Although a recent multicentric, retrospective study in Spain has shown that obese subjects with psoriasis have a poor therapeutic response to secukinumab,[4] no data are currently available for secukinumab in obese patients with PsA.

Our studies focused on the relationship between BMI and clinical response to secukinumab in PsA. We prospectively analysed 100 patients with PsA (57% female, median age 53 (49.2–55.0 years) satisfying Classification Criteria for Psoriatic Arthritis (CASPAR) criteria[5] for PsA, afferent to our clinics, who were treated with secukinumab. Patients were divided into two groups based on BMI (BMI<25 normal weight and BMI≥25 overweight/obese). In the normal-weight group, 75% were female; the median age was 50.5 (41.0–54.6); the median BMI was 22 (20.2–23.3); and the median Disease Activity in PSoriatic Arthritis (DAPSA) was 19.19 (15.6–24.2). The features of the overweight/obese patients were similar to those of the normal-weight group (48% were female, median age 54 (50–59), median BMI 29 (27.4–30.1) and median DAPSA 21.2 (19.0–24.4)). Clinical response to therapy, evaluated as the achievement of low disease activity or remission according to DAPSA, was recorded 6 months after starting treatment. After 6 months of treatment, the variation of the DAPSA was inversely related to BMI: overweight/obese patients had in fact a better response to secukinumab compared with normal-weight patients (figure 1A,B). By using a correlation coefficient (Statistical Package for Social Science (SPSS)) to analyse the degree of association between BMI and DAPSA, we confirmed that BMI and DAPSA were inversely related in patients with PsA (p=0.05) in our study.

Interestingly, analysis of serum levels of IL-17 in 20 obese patients compared with 20 non-obese patients showed significantly higher serum levels of IL-17 in the former (figure 1C), indicating IL-17 as a key cytokine driving inflammation in obese patients with PsA. As far as we are concerned, these are the first data about clinical response to secukinumab in obese patients with PsA. Obesity has been shown to promote the expansion of IL-17-producing T cells in adipose and peripheral tissues.[6] In addition, in patients affected by metabolic syndrome, the levels of IL-17R expression in the liver or muscles are correlated with insulin resistance.[6] Our results support the relevance of IL-17 in driving systemic inflammation in obese patients with PsA, also providing evidence that obese patients may have a better response to secukinumab compared with non-obese patients. Interestingly, this effect was not influenced by the secukinumab dosage. In conclusion, although further studies are required to confirm our data, these findings indicate a close relationship between IL-17, obesity and PsA, possibly supporting the idea that obesity might be one relevant clinical factor driving the choice of secukinumab in overweight/obese patients.

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A

			continuous BMI	DAPSA T6
Kendall's tau coefficient	Continuous BMI	correlation coefficient	1,000	0.135*
		1-TAIL SIGNIFICANCE	-	0.028
		N	100	93
	DAPSA T6	correlation coefficient	0.135*	1,000
		1-TAIL SIGNIFICANCE	0.028	-
		N	93	93
Spearman's rho	Continuous BMI	correlation coefficient	1,000	0.192*
		1-TAIL SIGNIFICANCE	-	0.032
		N	100	93
	DAPSA T6	correlation coefficient	0.192*	1,000
		1-TAIL SIGNIFICANCE	0.032	-
		N	93	93

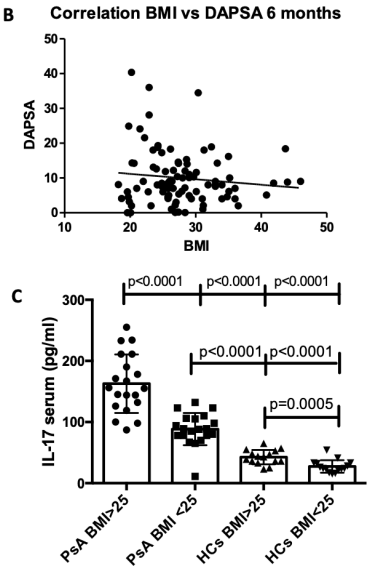

Figure 1 Correlation between BMI and DAPSA and serum IL-17 levels in PsA obese and non-obese patients. (A) Correlation between BMI and DAPSA by Kendall's tau coefficient and Spearman's rho tests (*statistical significance is for values of 0.05, one tail). (B) Graphical representation of correlation between BMI and DAPSA by Spearman test. (C) Analysis of serum levels of IL-17 in 20 obese and 20 obese and 20 non-obese patients compared to 30 healthy controls. BMI, body mass index; HC, health control; IL, interleukin; PsA, psoriatic arthritis.

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