Comment on: Different drug survival of first line tumour necrosis factor inhibitors in radiographic and non-radiographic axial spondyloarthritis: a multicentre retrospective survey

Sirs,

We read with great interest the recent paper by Lopalco *et al*. in which they compared the retention rate of the first tumour necrosis factor inhibitor (TNFi) in patients with radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) in real-world clinical practice (1).

In this retrospective cohort, the mean retention of first line TNFi was significantly higher among patients with r-axSpA than those with nr-axSpA (66.79 *vs*. 39.05 months, respectively). As the causes for discontinuation were comparable among the two groups, this suggests that TNFi were more effective in r-axSpA than in nr-axSpA. This is in contrast with the results of randomised clinical trials and observational studies which have shown comparable efficacy and effectiveness, respectively of TNFi in r-axSpA and nr-axSpA, at least in patients with objective signs of inflammation, *e.g*. elevated C-reactive protein or inflammatory lesions seen on magnetic resonance imaging (MRI) of the sacroiliac joints at baseline (4, 6, 7).

Some of the baseline characteristics, especially the age of symptom onset, HLA-B27 positivity, and diseases activity assessed by BASDAI of this cohort surprised us, as they differ significantly from prior reports. The age at the onset of symptoms was surprisingly high in the entire cohort, especially in the nr-axSpA group (46.65±13.99 years). The symptom onset in the GESPIC and DESIR cohorts for both r-axSpA and nr-axSpA were 36.1, and 33.0 years, respectively (2, 3). Additionally, a Swedish group has observed the symptom onset at the average age of 43, and 38 in r-axSpA, and nr-axSpA patients, respectively (4). The rate of HLA-B27 positivity was unexpectedly low, especially among the nr-axSpA patients (33.03%) when compared to 74.1%, and 86.4% in the DESIR, and Herne cohorts, respectively (3, 5). The BASDAI was significantly higher in nr-axSpA patients which is in contrast with several other cohorts that revealed comparable levels of BASDAI, and pain in AS or nr-axSpA patients (2, 3, 5).

Diagnosis of nr-axSpA is made based upon the clinician's judgement relying on the combination of symptoms, physical signs, laboratory and imaging findings present in an individual patient. These features can differ between patients, and the diagnosis requires exclusion of other potential causes of these abnormalities. Since the baseline characteristics of the patients in this cohort differ from historic cohorts one might question the diagnosis. It does not help, that the proportion of patients who had undergone magnetic resonance imaging of the sacroiliac joints, and the proportion of patients with an undetermined HLA-B27 status were not reported, especially as the proportion of HLA-B27 positive patients is so low.

In view of the relatively worse outcome in the nr-axSpA group, one may be tempted to speculate that in at least some of these subjects, chronic widespread pain was falsely interpreted as (active) SpA activity, thus contributing to the decision to start TNFi with no clinical benefits.

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