Persistence of ixekizumab in psoriatic arthritis and the influence of gender

Sirs,

Recently, Chimenti *et al*. have published the article entitled "Effectiveness of ixekizumab over 24 months in different clinical scenarios in psoriatic arthritis: results from the Gruppo Italiano Studio Early Arthritis multicentric prospective registry (GISEA)", published in *Clinical and Experimental Rheumatology* (1). It explores ixekizumab (IXE) treatment for psoriatic arthritis (PsA) and sheds light on treatment persistence and gender differences. In the cited article IXE proved to be equally effective in both genders after 24 months of treatment. However, men showed greater efficacy in terms of improvement in PASI and DAPSA remission at early follow-up (6 months), but the differences were equalised at 12 months. Women had a higher prevalence of fibromyalgia (38.6% *vs*. 7.1%) and more concomitant treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) (44.4% *vs*. 19.6%). IXE showed favourable pharmacologic survival rates, with retention rates of 67.4% at 24 months, slightly lower than those reported in a recent Spanish real-world multicentre observational PRO-STIP study by Joven *et al*. (2).

In another report, Braña *et al*. concluded that factors such as age, disease duration, female gender, smoking, obesity, metabolic comorbidities or previous exposure to other biologics did not affect drug persistence (3). Our working group has studied treatment persistence as an indicator of treatment efficacy and safety, and both qualities of a treatment are important when treating chronic diseases such as PsA. The greater discontinuation or switching of tumour necrosis factor inhibitor drugs (iTNF) in women than in men seems to be evident in different studies, but we do not know what happens with other biologics (4).

We conducted a multicentre observational study of patients with PsA undergoing iTNF and IXE treatment from January 1st 2022 to December 31st 2023. The objective was to evaluate persistence 52 weeks after initiation of iTNF and IXE and the influence of gender on persistence. We included 154 patients with PsA, these patients were mainly characterised by active and long-standing PsA (Table I).

They had an iTNF persistence of 78.6% *vs*. 84.1% for IXE (p=0.389), and treatment persistence was higher in men than in women in both groups (p=0.036 in the iTNF group and p=0.018 in the IXE group). Cox regression analysis showed that female gender was a predictor of treatment dropout throughout the 52 weeks of the study, and men had an OR of 2.768 (95%CI: 1.274–6.015) for persisting on treatment relative to women, p=0.010 (Fig. 1). We conclude that patients improved significantly in all parameters analysed over 52 weeks, with no significant difference between iTNF and IXE.

Patients treated with IXE had long disease progression and it was used after iTNF. Treatment persistence was high and there was a significant improvement in the PROs used. It could be observed that female gender was an independent factor for treatment discontinuation in the 2 treatment groups, iTNF and IXE, significantly, unlike the study by Chimenti *et al*. where treatment with IXE proved to be equally effective in both genders over time, with no significant differences in achieving remission of DAPSA or LDA.

In conclusion, these studies complement the knowledge on IXE in PsA, demonstrating its high persistence, but with slight advantages for men particularly in early response and lower dropout rate and persistence in women according to our results. Although women tend to discontinue treatment more frequently, other factors such as fibromyalgia or concomitant use of csDMARDs may influence persistence. These results underscore the importance of personalising management considering gender differences to maximise therapeutic outcomes and point to the need for more targeted research to address gender differences and optimise therapeutic strategies.

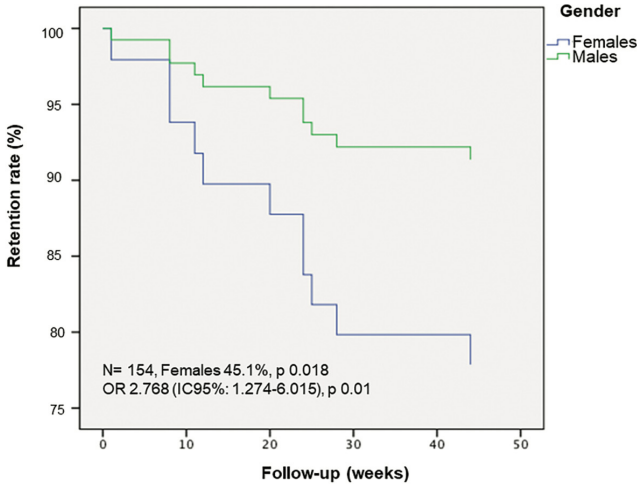

Fig. 1. Gender differences in 12-month retention rates in ixekizumab in patients with psoriatic arthritis.
Ixekizumab retention rates were estimated using the Kaplan-Meier estimator for both genders (females *vs*. males). Log-rank tests were used to determine differences in retention rates between the genders. The Cox proportional hazards models were used to calculate the weighted average of the hazard ratios (HRs) for ixekizumab treatment discontinuation over 12 months of follow-up.

Table I. Demographic characteristics.

Total, sample n (%)	154 (100)
Age, years (mean ± SD)	(56.7 ± 10.8)
Women n (%)	69 (45.1%)
Duration of PAs, years (mean ± SD)	9.6 ± 6.5
Peripheral involvement, n (%)	105 (69%)
Axial involvement, n (%)	10 (6.5%)
Mixed involvement, n (%)	38 (25%)
Enthesitis, n (%)	37 (25%)
Dactylitis, n (%)	14 (9.5%
Onychopathy, n (%)	38 (24.8%)
BSA, % (median, q1-q3)	1 (0-2)
BSA >3, n (%)	14 (9.2%)
NSAIDs, n (%)	63 (41.2%)
DMARD, n (%)	63 (41.2%)
Frequency of comorbidities, n (%)	
Hypertension	35 (31.2%)
Dyslipidaemia	28 (25.3%)
Obesity	23 (20.7%)

PAs: psoriatic arthritis; SD: standard deviation; BSA: body surface area; NSAIDs: non-steroidal anti-inflammatory drugs; DMARD: disease-modifying anti-rheumatic drug.

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