Efficacy and safety of ixekizumab in psoriatic arthritis: a retrospective, single-centre, observational study in a real-life clinical setting

Sirs,

Ixekizumab, a recombinant, humanised, monoclonal antibody, selectively binds and therefore neutralises IL-17A (1). A phase III randomised clinical trials (SPIRIT-P1) showed superiority of ixekizumab over placebo in moderate-to-severe psoriatic arthritis (PsA), in improving disease activity and inhibiting structural damage progression in patients treated with the anti-IL-17A monoclonal antibody for 52 weeks (2). Another phase III randomised clinical trial (SPIRIT-P2) was conducted exclusively on patients who had an inadequate response or intolerance to TNF inhibitors, demonstrating that ixekizumab determines a rapid improvement in the signs and symptoms of PsA (3, 4) and the contemporary amelioration of patient-reported measures of disease activity, generic and skin-specific HRQOL, and work impact of PsA on productivity (5).

A retrospective, observational study was conducted to assess the efficacy and safety of ixekizumab in patients affected by both moderate-to-severe plaque-type psoriasis (PsO) and moderate to-severe PsA in a real-life clinical setting.

We reviewed our clinical records and identified 26 outpatients (Group A) diagnosed with PsA and treated with ixekizumab for a moderate-to-severe cutaneous involvement who were placed in therapy at least 24 weeks before analysis. Among these patients, 17 (Group B) completed 48 weeks of treatment.

Demographic characteristics, clinical type and duration of Pso and PsA, presence of comorbidities and concomitant therapies, information on previous conventional or biological were collected from patients' medical files and added to the database.

Clinical parameters available at baseline, and for each visit, included Psoriasis Area and Severity Index (PASI) and Body Surface Area (BSA), to determine skin involvement. Likewise, visual analogue scale for pain (VAS Pain), tender joint count (TJC), swollen joint count (SJC), inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), presence of dactylitis (yes/no) and enthesitis (yes/no) and Disease Activity Index for Psoriatic Arthritis (DAPSA), a tool validated in 2010 for the assessment of PsA severity (6), were collected.

All the adverse events observed or referred by the patients and drop outs were recorded.

Statistical analysis was performed using the two-tailed Wilcoxon-Rinked-Signed test, comparing every parameter at baseline (BL) with those observed at week 24 (W24) and week 48 (W48). A *p*-value less than 0.05 was considered significant.

We evaluated 26 patients, 15 males (57.69%) and 11 females (42.341%) with an average age of 57.92 years (range 32.19-82.12) and an average BMI of 28.60 (range 22.72–36.73). Peripheral arthritis was present in 100% of the cases and axial disease coexisted in 11.54%. Enthesitis interested 33.33% of patients. Among co-morbidities, hypertension and cardiovascular diseases were those with greater incidence (57.69% and 23.07% of patients respectively), followed by diabetes (26.92%) and fatty liver disease (11.52%).

Only six patients (23.07%) were biologic-naïve, while the majority (76.92%) failed at least an anti-TNF-alpha inhibitor.

Concerning cutaneous manifestations, both PASI score and BSA extremely significantly improved since W24 ($p<0.00001$) (from 13.94 and 24.74 at baseline to 2.43 and 2.01 at W 24 respectively and from 14.07 and 24.57 at BL to 3.86 and 2.23 at W48 respectively) (Table I).

In particular, at W24 84.62% of patients achieved PASI75, 80.77% PASI90 and 57.69% PASI 100. At W48 82.35% of patients achieved PASI75, 70.59% PASI90 and 64.71% PASI 100.

Concerning PsA efficacy outcomes, the improvement from baseline to W24 was statistically significant for DAPSA ($p=0.0001$) (from 16.99 to 8.68), PAIN VAS ($p=0.0001$) (from 53.70 to 24.35), and TJC score ($p=0.00328$) (from 3.74 to 1.39). At W48 the improvement was statistically significant for DAPSA ($p=0.00288$) (from 19.83 to 9.71), PAIN VAS ($p=0.0114$) (from 55.71 to 27.14), and SJC score ($p=0.00672$) (from 2.21 to 0.07) (Table I).

All other clinical variables evaluated showed a progressive reduction, but not statistically significant. Ixekizumab was found to be safe and well tolerated. Two episodes of injection site reactions appear to be the only adverse events experienced and did not require discontinuation of therapy.

At W24, two patients withdraw from treatment because of lack of efficacy on skin disease.

Table I. Improvement of psoriatic arthritis severity scores from baseline to week 24 (Group A) and from baseline to week 48 (Group B) with relative statistical significance.

	GROUP A (26 patients)			GROUP B (17 patients)		
	Baseline	Week 24	*p-value*	Baseline	Week 48	*p-value*
Mean PASI	13.94	2.43	<0.00001	14.07	3.86	<0.00001
Mean BSA	27.74	2.01	<0.00001	24.57	2.23	0.00046
Mean PAIN VAS	53.70	24.35	0.0001	55.71	27.14	0.0114
Mean TJC	3.74	1.39	0.00328	5.43	2.64	ns
Mean SJC	1.43	0.78	ns	2.21	0.07	0.00672
Mean ESR	25.70	19.35	0.02088	22.14	24.29	ns
Mean CRP	1.73	1.27	ns	1.93	5.21	ns
Mean DAPSA	16.99	8.78	0.0001	19.83	9.71	0.00288

PASI: Psoriasis Area and Severity Index; BSA: body surface area; PAIN VAS: visual analogue scale for pain; TJC: tender joint count; SJC: swollen joint count; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; ns: non-significant.

This study showed a good effectiveness of ixekizumab both on skin lesions and on articular symptoms, in patients affected by moderate to severe PsA.

A high proportion of patients at six months achieved a skin clearance that was maintained over time. Likewise, a low disease activity of arthritis was reached rapidly within the first 6 month of treatment, with a sustained efficacy during the 12 months of the follow-up period.

Moreover, ixekizumab demonstrated a very good safety profile, with no serious adverse events in all the patients treated.

Despite the limitations of our study (in particular, the low sample size, a limited follow-up and all patients received the higher Pso indicated dose regimen), our results suggest ixekizumab to be effective, either in plaque-type psoriasis or in psoriatic arthritis, being all considered parameters significantly improved over treatment.

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