Interstitial lung involvement in rheumatoid arthritis patients treated with abatacept

Dear Editors,

We have read with interest the paper by Vacchi *et al.* recently published in *Clinical and Experimental Rheumatology* (1). This prospective multicentre observational cohort of 325 patients with rheumatoid arthritis (RA) treated with abatacept, with or without interstitial lung disease (ILD), shows lung function and radiological evolution as well as ILD incidence, respectively, after two-year follow-up (1). The paper reports some results that we believe are worth commenting on.

RA-ILD prevalence (20.6%) pointed out by Vacchi *et al.* (1) is in line with a recent observational study conducted in 15 Spanish hospitals that found a 13% prevalence of RA-ILD on high-resolution computed tomography and 8.3% subclinical ILD (2).

However, incident rates of new-onset ILD (two cases) seem strikingly low, especially considering the analysed period was coincident with the COVID-19 pandemic, due to the described association between SARS-CoV-2 infection and the incidence or worsening of ILD related to systemic autoimmune diseases (3).

The lack of relationship of ILD incidence with anti-citrullinated protein antibodies and RA severity parameters, such erosions and extra-articular manifestations, is remarkable as this association has been repeatedly reported in literature. We also miss a mention of the role of disease activity, especially when persistent, which has also been linked to a higher incidence of RA-ILD (4). The longer duration of RA in the non-ILD group compared to the ILD group, and the higher proportion of the non-specific interstitial pneumonia (NSIP) pattern (74.6%) than the usual interstitial pneumonia (UIP) pattern (25.4%), are also contrary to literature reports. In a Spanish series including 263 RA-ILD patients, ILD distribution was: UIP 40.3%, NSIP 31.9%, other patterns 27.8% (5). This fact could have undoubtedly influenced the better lung evolution of the series by Vacchi *et al.* compared to other cohorts (6).

Regarding methotrexate (MTX) treatment, the information provided in the text contradicts that shown in Table I. While the authors report a lower MTX use in ILD *versus* non-ILD patients, the table shows significantly higher frequency of MTX use in the former (46.3% *vs.* 29.8%, respectively). Interestingly, the longer duration of abatacept therapy in non-ILD patients could suggest its potential preventive role on ILD development.

An interesting point is the utility of VECTOR device, a digital tool for early detection of 'velcro crackles'. Validating it in other populations and comparing its efficiency for early screening of RA-ILD with other techniques as lung ultrasound would be worthwhile.

Another outstanding point discussed by Vacchi *et al.* (1) is the efficacy of targeted synthetic DMARDs in refractory cases of RA-ILD. It is in accordance with the favourable efficacy and safety profile of baricitinib reported in a multicentre retrospective study of 72 RA-ILD patients, both for pulmonary and joint manifestations, even in refractory patients (7).

Additionally, Vacchi *et al.* do not provide information regarding potential differences according to abatacept administration route, abatacept monotherapy *versus* combined with MTX, or radiologic pattern. In this regard, in a study including 190 patients with UIP and NSIP patterns, abatacept was associated with similar stability of lung function and radiologic involvement in both groups (8). Furthermore, in a cohort of 263 RA-ILD patients, abatacept in monotherapy or combined with MTX yielded comparable outcomes, although combination therapy showed a clearer corticosteroid-sparing effect (9). These data, together with findings from a multicentre cohort of 526 RA-ILD patients suggesting a potential pulmonary 'window of opportunity' for abatacept (10), may help contextualise the therapeutic interpretation of the study by Vacchi *et al*. (1).

In conclusion, we believe that Vacchi's data are very stimulating, although there may be some peculiarities of the included population that differ from other series published to date, and influence the results to some extent.

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