Reply to: Interstitial lung involvement in rheumatoid arthritis patients treated with abatacept

Dear Editors,
We thank Vicente-Rabaneda *et al.* for their interesting letter (1) and we would like to also congratulate them, because they substantially expand the evidence on this topic with the description of other experiences, mainly from Spain. Among their observations, they pointed out on the low incidence rate of interstitial lung disease (ILD) in our population of rheumatoid arthritis (RA) patients treated with abatacept (2).
In a Danish population study, Hyldgaard *et al.* reported that approximately 75% of RA-ILD were diagnosed within 5 years from RA onset (3). Since RA-ILD patients may remain asymptomatic for a long period of time, many cases could be diagnosed later over the disease course, after the occurrence of clinical symptoms (4). Therefore, the incidence of RA-ILD may appear higher in patients with established disease in the absence of systematic screening of the patients.
In our study, at enrolment, each patient was evaluated by VECTOR (5), a software able to identify velcro crackles in respiratory sounds, and 6 RA-ILD asymptomatic patients were thus diagnosed. Systematic screening allows identifying patients in a preclinical stage, thereby reducing the number of subsequent new diagnoses. Detection of respiratory sounds is currently the only validated biomarker useful for the screening of RA-ILD (6), although different diagnostic algorithms have been proposed (4, 7).
Our results have not shown any correlation between ILD incidence and anti-citrullinated protein antibodies (ACPA) or RA severity parameters, such as erosions and extra-articular manifestations (3, 5). This is not surprising, since our population was not representative of the overall population of RA, but only of Italian RA patients treated with abatacept. In this regard, ACPA positivity is one of the main drivers for the prescription of abatacept in RA patients (8), regardless of the coexistence of ILD, that could have represented a further factor for the choice of the drug according to the available literature (9).
Our study was not designed to assess the role of RA disease activity as a risk factor for ILD. In fact, our patients had already been receiving abatacept for at least three months before enrolment; consequently, patients' disease activity was generally well controlled, otherwise abatacept would probably have been withdrawn. Disease activity has been proposed as a risk factor of RA-ILD in some studies (10), but it is difficult to assess it in RA patients receiving effective treatment and regularly managed according to the treat-to-target approach (8).
Similarly, the distribution of radiologic ILD patterns did not reflect the real-world characteristics of RA-ILD (6), but it only mirrors the therapeutic choices of Italian rheumatologists in this population.
According to Vicente-Rabaneda *et al.* (1), undoubtedly the prevalence of non-specific interstitial pneumonia in our cohort could have contributed to the good results observed. In any case, abatacept stabilised or improved RA-ILD with UIP pattern in 70% of our cases, although the absence of a control group and of other prospective studies evaluating abatacept in RA-ILD patients does not allow any definitive conclusions regarding this point.

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