Correspondence on 'Tapering towards DMARD-free remission in rheumatoid arthritis'

We believe that the article 'Tapering towards DMARD-free remission in established rheumatoid arthritis: 2-year results of the TARA trial' by Mulligen *et al*,[1] is of great interest since it addresses important information on the gradual reduction of treatment in patients with rheumatoid arthritis (RA), to achieve disease-modifying antirheumatic drug (DMARD)-free remission (DFR). However, we would like to highlight and complement the importance of some potentially relevant points, and broaden the horizon and the approach to a topic of such complexity:

1. Although the 'European League Against Rheumatism (EULAR) 2019 recommendations on the management of RA suggest a gradual decrease in glucocorticoids prior to the reduction of DMARD in patients with sustained complete remission, it also refers the possible therapeutic benefits of their concomitant use at very low doses (1–3 mg of prednisone (PDN)), if there are no unacceptable adverse events.[2] This is also suggested in a study by Buttgereit *et al*[3] that evaluated 350 randomised patients with RA assigned to 5 mg of PDN plus DMARD versus placebo plus DMARD; they detected greater responses in ACR20, ACR50 and improvement in pain, fatigue, stiffness and function with the use of low doses of glucocorticoids. Hence, this could be a therapeutic strategy fostering a decrease in the rate of exacerbations during DMARD withdrawal.
2. The authors mentioned in their discussion that 30% of the group that initially decreased conventional synthetic DMARD (csDMARD) and 45% of the group that first decreased the TNF-inhibitor (TNFi) were not on monotherapy[1]; therefore, at the time of remission, they were still treated with some other DMARD, thus precluding absolute results of sustained remission free of DMARD, the study's main objective. Comparing the characteristics of patients only on monotherapy would be desirable.
3. The low percentage of patients who achieved sustained remission, 31% in the group that first decreased csDMARD and 21% in the TNFi group, is replicated in various systematic reviews such as those by Verstappen *et al*[4] that reported DFR in 5% and 24.3% less than 12 months after DMARD withdrawal, and between 11.6% to 19.4% after more than 12 months. Exacerbations developed frequently during the DMARD taper (41.8%–75%), and in the first year after achieving DFR (10.4%–11.8%). Many patient characteristics lacked an association with DFR; however, the absence of autoantibodies and shared epitopes increased the possibility of achieving DFR, which is why we believe it is relevant to know the characteristics of the patients' disease course, including failure to achieve sustained remission with previous treatments, disease duration and the positivity of antibodies. It is also noteworthy that in studies such as Boeters *et al*[5] that evaluated 299 patients with anti-citrullinated protein antibody (ACPA)-negative RA, C reactive protein (CRP), serum amyloid A and matrix metalloproteinase 3 were individually associated with sustained DFR.
4. Another important point in the evaluation of sustained remission free of DMARD is the use of joint ultrasound or MRI to corroborate the absence of synovitis and thus, treatment decreases with a lower risk of exacerbations. This has been corroborated in studies such as that of Geng *et al*[6] that evaluated 111 patients with RA in clinical remission, of which 110 (99.1%) were in complete remission by disease activity score 28 (DAS28) CRP, 76 (60.4%) by DAS28 erytrosedimentation rate (ESR), 55 (49.5%) by clinical disease activity index (CDAI), 50 (45%) by simplified disease activity index (SDAI) and 54 (48.6%) by American College of Rheumatology/EULAR; power Doppler ultrasonography revealed subclinical synovitis in 57 (51.8%), 30 (44.8%), 22 (40%), 19 (39 %) and 18 (33.3%). These results led to modifications in the DMARD dose to decrease the risk of exacerbations.

Due to the polyarticular characteristics of the disease, it is difficult to consider that patients only have one inflamed joint at the time of DFR, but they were included following the selection criteria in the article by Mulligen *et al*[1]; the lack of power Doppler ultrasonography precludes the definite lack of more inflamed joints and increases the probability of exacerbations.

We believe that achieving DFRs in patients with RA remains a challenge. However, power Doppler ultrasonography and strategies such as the continuous use of very low doses of glucocorticoids could decrease the rate of exacerbations.

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