Response to: 'Correspondence on 'EULAR recommendations for the management of antiphospholipid syndrome in adults' by Zhou *et al*

We thank Zhou *et al*¹ for their interest in the 2019 European League Against Rheumatism (EULAR) recommendations for the management of antiphospholipid syndrome (APS) in adults.²

Although glucocorticoids (GC) are widely used in systemic lupus erythematosus-associated APS, there is some uncertainty about their use in primary APS, and more specifically, about their use and dosage in the second and third trimester of pregnancy. In the EULAR recommendations for APS management, the use of GC in patients with primary APS is recommended only in catastrophic APS (CAPS), and may be considered in refractory cases of obstetric APS at low-doses (≤ 10 mg prednisolone daily) and for only the first trimester.² The latter statement is based on expert opinion due to the limited evidence. The only retrospective cohort study that addressed this question is described in the accompanying article with the results of the systematic literature review (SLR) informing the EULAR recommendations.³ This study compared the pregnancy outcomes between women treated with a combination with low dose aspirin and heparin, with or without the addition of prednisolone 10 mg/day which was discontinued at week 14 of gestation.⁴

In their second point, Zhou *et al* note some issues related to the feasibility of a diagnosis of CAPS in clinical practice. The 2019 EULAR recommendations include statements about the management of APS patients based on the currently available classification criteria for APS and for CAPS. The statement for the management of CAPS refers to patients with definite CAPS based on the McMaster RARE-Best practices guidelines for CAPS management.⁵ Consideration of revising the classification criteria for CAPS was beyond the scope of these recommendations.

Zhou *et al* have also commented that EULAR recommendations 'did not recommend the choice of disease-modifying antirheumatic drugs (DMARDs) in severe cases, and whether there is a preference'. According to the current evidence, the use of DMARDs was discussed only for patients with refractory CAPS. The following statement was included in the table of recommendations which was graded as 4/D since it was based only on case reports: 'In patients with refractory CAPS, B cell depletion (eg, rituximab) or complement inhibition (eg, eculizumab) therapies may be considered'.² Ongoing studies have shown that inflammatory and thrombotic mechanisms coexist in APS and the role of immunoregulatory agents in APS, especially in refractory APS, is under investigation.⁶

Another question raised was whether 'there is a high-priority for GC and plasma exchange or intravenous immunoglobulins in patients with high-risk antiphospholipid antibody (aPL) profiles and new-onset thrombosis, besides heparin'. Currently, there is no evidence to support the use of GC and plasma exchange or intravenous immunoglobulins after a thrombotic event in patients with high-risk aPL profile, except the case of definite CAPS.

Finally, the use of aspirin in women with positive medium-high aPL titres but with just one or two spontaneous miscarriages (<10 th week), not meeting the APS classification criteria, was addressed by the corresponding recommendation in Table 1 and the text (section 8.C, page 6).² Additionally, in the publication of the results of the SLR informing the EULAR recommendations,³ there is a specific section about the 'Treatment of women with a history of two recurrent spontaneous abortions <10 th week of gestation'. The task force agreed that treatment with low dose aspirin alone or in combination with heparin might be considered

based on an individual's risk, but this statement was mainly based on expert opinion due to limited evidence since the majority of studies combined several types of pregnancy losses without specifying on 'non-criteria' APS. The presence of only one spontaneous miscarriage <10 th week of gestation was not included in our search since there is no evidence that this sole manifestation might support the suspicion of obstetric APS.

We agree that more evidence is needed to adequately address these questions in the future, hopefully in the update of the EULAR recommendations for the management of APS in adults.

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