Response to: 'Clinical evidence guidelines in systemic lupus erythematosus: revaluation' by Scheinberg

We want to thank Dr Morton Scheinberg for his interest[1] in our recent lupus guidelines communication.[2] In his letter, he points out several concerns regarding belimumab which we had recommended at the same therapeutic level as other immunosuppressants for joint and skin manifestations. Few clarifications are needed.

The development of our guidelines followed a rigorous methodology in which the evidence on effect estimates should come, when available, from randomised controlled trials (RCTs). We did not identify any clinical trial comparing belimumab against other immunosuppressants. Therefore, in considering this comparison, the development group had to rely on indirect evidence (the difference in belimumab effect against placebo and other immunosuppressants against placebo) or high risk of bias evidence (from observational studies). In this context, the panel agreed that the certainty that belimumab was better (or worse) than other immunosuppressants was low/very low and therefore decided not to recommend one over the others.

Dr Scheinberg emphasised that in constructing the recommendation we missed relevant information; nevertheless, he did not provide any additional data that could justify this affirmation (RCT about the effects of belimumab in comparison with other immunosuppressants), instead he referenced a non-comparative observational study,[3] an RCT that was included in our review and considered in constructing the recommendations[4] (the reference provided was from a longer follow-up timeframe that was published after the systematic search of our guideline was finished whose results confirmed earlier findings), and a cost-effectiveness analysis that did not model belimumab against other immunosuppressants[5] (only modelled belimumab as add-on therapy) and was based on the information of the BLISS trials,[4 6] also included in our review. We acknowledge that not providing a recommendation (between different immunosuppressants) could not be the best of the guidance as, in practice, guideline users need to decide which one to prescribe; nevertheless, we agreed that in the absence of a head-to-head RCT, a conservative approach (providing the evidence and panel judgements without a recommendation) was the best way to proceed.

We are glad that Dr Scheinberg is concerned about the side effects of glucocorticoids as we do. For that reason, we have emphasised this as an overarching principle.

Finally, the letter mentions difficulties on expert consensus methodology.[7] We agree and have intensively lived that experience in the past. That is why, for these guidelines, we had decided to incorporate a transparent guideline development methodology in which the recommendations were intended to be based on the best available evidence such as the Grading of Recommendations Assessment, Development and Evaluation system, just as described in the editorial.[7]

We very much appreciate Dr Scheinberg's encouraging and insightful comments. We eagerly await new strong clinical evidence of current and new therapeutic options for our patients with lupus.

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REFERENCES

1 Scheinberg M. Clinical evidence guidelines in systemic lupus erythematosus: revaluation. *Ann Rheum Dis* 2018. doi: 10.1136/annrheumdis-2018-214357. [Epub ahead of print: 25 Sep 2018].
2 Pons-Estel BA, Bonfa E, Soriano ER, *et al*. First Latin American clinical practice guidelines for the treatment of systemic lupus erythematosus: Latin American Group for the Study of Lupus (GLADEL, *Grupo Latino Americano de Estudio del Lupus*)–Pan-American League of Associations of Rheumatology (PANLAR). *Ann Rheum Dis* 2018. doi: 10.1136/annrheumdis-2018-213512. [Epub ahead of print 25 Jul 2018].
3 Fanouriakis A, Adamichou C, Koutsoviti S, *et al*. Low disease activity—irrespective of serologic status at baseline—associated with reduction of corticosteroid dose and number of flares in patients with systemic lupus erythematosus treated with belimumab: a real-life observational study. *Semin Arthritis Rheum* 2018. doi: 10.1016/j.semarthrit.2018.02. [Epub ahead of print 23 Feb 2018].
4 Furie RA, Wallace DJ, Aranow C, *et al*. Long-term safety and efficacy of belimumab in patients with systemic lupus erythematosus: a continuation of a seventy-six-week phase iii parent study in the United States. *Arthritis Rheumatol* 2018;70:868–77.
5 Díaz-Cerezo S, García-Aparicio ÁM, Parrondo J, *et al*. [Cost-effectiveness analysis of Belimumab in patients with systemic lupus erythematosus in Spain]. *Farm Hosp* 2015;39:161–7.
6 Navarra SV, Guzman RM, Gallacher AE, *et al*. Belimumab, a BLyS-specific inhibitor, reduced disease activity, flares and prednisone use in patients with active SLE: efficacy and safety results from the phase 3 BLISS-52 study. *Lancet* 2011;377:721–31.
7 Barosi G, Gale RP. Is there expert consensus on expert consensus? *Bone Marrow Transplant* 2018;53:1055–60.