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# The stratification of primary Sjogren's syndrome: is it really solving the problem?

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Dear Editor,

I read with interest the paper of Collins et al. concerning the reanalysis of the JOQUER trial using the four pathobiological groups of patients with Sjogren's syndrome [1]. This division of Sjogren in four phenotypes could solve the problem of complexity and heterogeneity which complicates the choice of an appropriate outcome. These phenotypes were obtained by statistical means, and were possibly confirmed by the differences found between these groups concerning biological, including transcriptional, determinations, and validated on two independent cohorts of patients [2].

Reanalyzing the results of the JOQUER trial, it was shown that hydroxychloroquine might be effective in both subgroups of patients with high and low symptom burden, and not effective in the subgroups of pain dominant, and dryness dominant with fatigue patients.

The discovery of these subgroups could be an important step ahead for the clinical management and trial design concerning the patients with Sjogren's syndrome. However, the efficacy of the drug both in the high burden, and low burden symptoms group is counterintuitive, and the most probable explanation is chance. Moreover, the previous reanalysis of the same trial, using the same subgroups, but in another article [2] found effectiveness only in the high symptom burden group.

The reanalysis showed that, in the high symptom burden group, the relative improvement of ESSPRI between hydroxychloroquine and placebo at 24 months was of 1.49 points (95% CI 0.54–2.43). This is a statistically significant difference. However, the authors did not demonstrate that the difference was clinically significant, too, as the minimally important difference of 1 point on ESSPRI [3] was inside the confidence interval.

Thus, there still is a long way to go until the possible validation of this stratification.

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