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Patients with systemic lupus erythematosus using hydroxychloroquine or chloroquine develop severe COVID-19 at similar frequency as patients not on antimalarials: need to explore antithrombotic benefits for COVID-19 coagulopathy

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We thank Carbillon et al. for their correspondence[1]. The use of hydroxychloroquine (HCQ) in pregnant women with systemic lupus erythematosus (SLE) is not controversial[2,3]. Similar to its primary role in the prophylaxis and treatment of SLE, discontinuation of HCQ in pregnancy has been linked to increased disease activity and glucocorticoid use in women with lupus[4–6]. Given its benefit and preferable safety profile, the continuation of baseline HCQ therapy in pregnant women with lupus is recommended to maintain disease remission[2,3], regardless of SARS-CoV-2 status. In contrast, there is currently no evidence to suggest that baseline use of HCQ in pregnant women with lupus is protective of SARS-CoV-2 infection or severe Coronavirus disease 2019 (COVID-19).

The authors adequately summarize our findings that patients with lupus – even if they are using an antimalarial such as HCQ as baseline therapy – can develop SARS-CoV-2 infection and severe COVID-19 at similar frequency as patients not on antimalarials[7]. We agree that unequal distribution of comorbidities and disease-modifying anti-rheumatic drug (DMARD) therapy have to be considered as sources of confounding, and statistical correction for such variables may be informative as sample size increases. In a recent publication by the COVID-19 Global Rheumatology Alliance examining 600 rheumatic disease patients with COVID-19, 22% were taking antimalarials prior to hospitalization[8]. No significant association between baseline antimalarial use and hospitalization was

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observed after adjusting for sex, age over 65 years, smoking status, underlying rheumatic disease, comorbidities, conventional synthetic (cs)-DMARD monotherapy, biological(b)/targeted synthetic(ts)-DMARD monotherapy, csDMARD- b/tsDMARD combination therapy (excluding antimalarials), use of NSAIDs, and glucocorticoid dose (OR=0.94, 95% CI 0.57–1.57; *P*=0.82)[8]. The null effect remained in additional models controlling for disease activity. In light of these findings, but also acknowledging the innate limitations of observational and physician-reported data, patients with lupus on HCQ do not appear to be protected from severe COVID-19. We await the results of ongoing randomized, controlled trials to clarify whether HCQ has any role in the prophylaxis or treatment of COVID-19.

Adding to these clinical data, we provide a pharmacokinetic rationale why antiviral properties of HCQ at doses commonly prescribed in lupus (400 mg daily or less) are not expected to be protective of SARS-CoV-2 infection[7]. Importantly, this does not preclude potential benefits of HCQ for the hypercoagulable state observed in some patients with COVID-19. While HCQ has been shown to be protective against arterial and venous thrombosis in SLE[9,10], extrapolating these benefits to the coagulopathy of COVID-19 is premature. Ongoing controlled trials of HCQ in non-lupus patients will likely be informative to explore potential antithrombotic benefits for COVID-19 coagulopathy.

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