Response to: 'COVID-19 among Malaysian patients with systemic lupus erythematosus on hydroxychloroquine' by Teh *et al*

We thank Teh *et al* for their interest in our study reporting on the course of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) COVID-19 in a case series of patients with systemic lupus erythematosus (SLE) under long-term treatment with hydroxychloroquine (HCQ).[1 2] Teh *et al* report in detail the clinical course of COVID-19 in five patients with SLE in Malaysia. All patients were women, 50 years old on average, under long-term HCQ treatment, and the majority were suffering from comorbidities such as hypertension, obesity or diabetes. All patients presented with moderately severe to severe COVID-19; one patient died and another needed invasive ventilation. In this respect, the series of patients with SLE infected with SARS-CoV-2 described by Teh *et al* resemble other series previously reported by our group and others, encompassing a low number of patients, often hospitalised, with a majority of women in their 50s suffering from various comorbidities and an occasional severe or even lethal clinical evolution.[1 3] However, these case series do not allow drawing of conclusions on the incidence rate and severity of COVID-19 in SLE, because they most likely over-represent the most symptomatic and severe cases, resulting from a selection bias because of clinicians tending to report the most dramatic cases. The results from these series nevertheless point to a lack of a preventive effect of HCQ, at least in these patients, and suggest, similar to what has been observed in the general population, that comorbidities favour the severity of COVID-19 in patients with SLE.[1–3] Recent investigations with different study designs now complete these data by giving an estimation of the incidence of COVID-19 and its severity in patients with SLE. In a cohort of 165 patients with SLE in Italy, Bozzalla Cassione *et al* reported a prevalence of 7.2% of confirmed or suspected COVID-19, with a disease course that was generally mild with only one patient requiring intensive care, subsequent to the development of acute respiratory distress syndrome.[4] In another cohort of 225 patients with SLE in Belgium, Gendebien *et al* reported a prevalence of 8% of confirmed or suspected COVID-19, with only two patients hospitalised without the need for intensive hospital care.[5] A third case series from New York City has suggested that 18 (4%) of the 450 patients with SLE, followed-up in the Colombia Lupus Cohort, developed symptomatic confirmed or clinically suspected COVID-19, as compared with the suggested 2% community risk in New York City.[6] Clinical symptoms of COVID-19 were more pronounced than in the previous two studies with seven patients being hospitalised and three suffering from severe hypoxaemic respiratory failure, two of whom required non-invasive ventilation and one required invasive mechanical ventilation.[6] In this cohort, 83% and 39% of the patients with COVID-19 with SLE were taking immunosuppressants or steroids, respectively, prior to infection with SARS-CoV-2, which was substantially more than in the cohorts reported by Bozzalla Cassione *et al* and Gendebien *et al*.[6] The authors also noted a high frequency of lupus nephritis. In these three studies, no risk factors for contracting COVID-19 or developing a severe form of the disease were clearly identified. However, given that the vast majority of the patients with SLE included in these three cohorts were taking either HCQ or chloroquine, the effectiveness of these treatments to prevent symptomatic COVID-19 in SLE has been questioned.[4–6]

We believe the available information from the studies published as yet warrants the conclusion for now that the incidence of COVID-19, both severe and non-severe, is not dramatically increased in patients with SLE, as compared with the general population or with patients with rheumatic diseases. Furthermore, the first results obtained from patients with COVID-19 with immune-mediated inflammatory disease seem to indicate that exposure to prednisone without dose precision,[7] or at doses exceeding 5 mg/day[8] or 10 mg/day,[9] as well as the use of methotrexate[7 8] and rituximab[8] are associated with hospital admission. In one study, a prednisone dose exceeding 5 mg/day was reportedly associated with mortality.[8] However, at present, these observations cannot be extended to SLE. Future studies dedicated specifically to this disease will eventually determine the non-specific and specific risk factors that contribute to the development of a severe form of COVID-19 in SLE.

Alexis Mathian , **Zahir Amoura**

Sorbonne Université, Assistance Publique–Hôpitaux de Paris, Groupement Hospitalier Pitié–Salpêtrière, French National Referral Center for Systemic Lupus Erythematosus, Antiphospholipid Antibody Syndrome and Other Autoimmune Disorders, Service de Médecine Interne 2, Institut E3M, Inserm UMRS, Centre d'Immunologie et des Maladies Infectieuses (CIMI-Paris), Paris, France

Correspondence to Dr Alexis Mathian, Internal Medicine, University Hospital Pitié Salpêtrière, 75651 Paris, France; alexis.mathian@aphp.fr

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ORCID iD
Alexis Mathian http://orcid.org/0000-0002-7653-6528

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