Still early to define a clear role of antimalarial drugs for COVID-19 in patients with rheumatic disease. Response to: 'Hydroxychloroquine reduces the risk of covid-19 in patients with rheumatic diseases: myth or reality?' by Xie *et al*

We thank Xie *et al*[1] for the interest in our letter[2] and found some relevant points to discuss the role of antimalarial drugs during the COVID-19 pandemic. The information has increased at an incredible rate since our letter was published. Despite initial encouraging in vitro and preclinical studies, current evidence supporting the role of antimalarial drugs for prophylaxis or treatment of COVID-19 has been predominantly contradictory or negative.[3]

COVID-19 was classified as a pandemic on 11 March 2020 by WHO.[4] To this date (7 June 2020), 6 799 713 cases have been confirmed worldwide, with 397 388 deaths.[5]

The severity and mortality of this virus have motivated researchers to find an effective treatment. Many prophylaxis (pre-exposure and postexposure) trials are currently running. Boulware *et al* conducted a randomised, double-blind trial in the USA and Canada that tested postexposure prophylaxis with hydroxychloroquine (HCQ) or placebo. They included 821 asymptomatic participants with moderate or high-risk exposure to receive within 4 days of the exposure HCQ or placebo, no significant difference in the rate of confirmed or probable COVID-19 were found between groups, side effects were more frequent in the HCQ than in the placebo group, but no serious adverse events were reported.[6] Some limitations of the report included the low number of PCR-confirmed cases, the recruitment methodology, the participant-reported data and the variable time to start HCQ.[7]

A systematic review of antimalarial drugs in COVID-19 concluded that current evidence is weak, insufficient and conflicting. The review included 4 randomised controlled trials, 10 cohort studies and 9 case series. Adverse events information from the studies included was also limited to draw solid conclusions and evaluate the risk–benefit of these interventions.[3]

In an observational study of hospitalised patients with COVID-19, HCQ administration was not associated with decreased intubation or death.[8] Recently, a study that demonstrated an inefficient response with the use of antimalarial drugs to treat COVID-19 and showed an increased risk of de novo ventricular arrhythmias retracted from these findings, only demonstrating the need to continue research on the subject and the risk of taking therapeutic decisions with these early results.[9]

The COVID-19 Global Rheumatology Alliance system has reported 2102 provider registration cases and 12 499 patient's survey registration cases of COVID-19 in rheumatic patients.[10] The first report including 600 patients with rheumatic disease with confirmed COVID-19 from 40 countries showed that 46% were hospitalised and 9% died. The most common diagnoses were rheumatoid arthritis (38%) and systemic lupus erythematosus (SLE) (14%). Patients with SLE (OR 1.8), vasculitis (OR 1.56) and axial spondyloarthritis (OR 1.11) were at increased risk of hospitalisation. Higher rates of hospitalisation were associated with older age and comorbidities (hypertension, lung disease, diabetes, cardiovascular disease and chronic kidney disease). The use of prednisone (>10 mg/day) was also associated with an increased risk of hospitalisation. Anti-TNF use was associated with decreased hospitalisation rates (OR 0.4) independently on antimalarial drug use (OR 0.94).[11 12]

The EULAR and ACR groups have suggested several recommendations in the use of antimalarial drugs, stating to continue this treatment if this were given previously, not augmenting the dose as prophylaxis or treatment of COVID-19, and not implementing the use of these drugs for this reason.[13 14]

With all this previously portrayed, we continue to think that it is still early to define a clear role of antimalarial drugs for COVID-19 treatment in patients with rheumatic disease and consider more studies should be performed before recommending the implementation of these drugs in our clinical practice as prophylaxis or treatment. Hopefully, as clinical evidence accumulates, the real risk our rheumatic patients have will become clearer.

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Handling editor Josef S Smolen

Contributors CMG-A, GF-P and DAG-D drafted and revised the manuscript for important intellectual content.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

CMG-A and GF-P contributed equally.

To cite Gamboa-Alonso CM, Figueroa-Parra G, Galarza-Delgado DA. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-217633

Received 9 June 2020
Revised 10 June 2020
Accepted 12 June 2020

► https://doi.org/10.1136/annrheumdis-2020-217556

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-217633

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