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## Letter Cyclosporine A and COVID19 – The COQUIMA cohort

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However interesting, results from the COQUIMA study arguing for the beneficial effect of cyclosporine in severe COVID19 pneumonia have some inconsistencies precluding a correct interpretation [1]. Considering that patients with therapeutic effort limitations were excluded from the analysis, it is inferred that the ICU-admitted patients reflected the most severe subgroup of the cohort. In fact, mortality rate in this subgroup approached 49%. This incidence is far from the 17% stated at the manuscript, the latter corresponding to the contribution of these deaths to the whole cohort's mortality. Thereby, it appears paramount to separately analyse survival in patients who did not require admission to the ICU, moreover considering that cyclosporine was withdrawn upon ICU admission. Strikingly, information regarding the percentage of ICU-admitted patients who were exposed to cyclosporine is missing. Besides, if severe cases are the target population, not only patients with extremely bad prognosis, but also mild cases being discharged shortly after admission should be filtered out. Even though these corrections might lower the effect size of the intervention, they would surely provide accurate insight into the role of cyclosporine in the management of COVID19.

As we have elaborated on and also has been pointed out by Dr Guisado-Vasco, cyclosporine may short-circuit pivotal viral activities and provide mitochondrial protection from stress, the latter being presumably required for an efficient response against SARS-COV2 [2]. On the other hand, I would suggest that inhibition of NF $\kappa$ B should not be considered a straightforward cyclosporine-dependent action in this disease and in fact there could be a rationale for a combined strategy with cyclosporine and NF $\kappa$ B blockage in the treatment of COVID19's inflammatory syndrome.

#### **Declaration of Competing Interest**

Dr. SANCHEZ-PERNAUTE reports to be conducting a nonprofit RCT (NCT04392531) of cyclosporine A in COVID19 pneumonia.

#### References

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