LETTER TO THE EDITOR

CYP450 3A4/5 Containment During SARS-CoV-2 Infection

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To the Editor:

We read with great attention the recent article by Le Carpentier *et al.*[1] regarding the impact of acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection on midazolam metabolism in patients with severe coronavirus disease 2019 (COVID-19). The results presented in this study confirm the general picture already drawn by us and others regarding the impact of inflammation on cytochrome P450 (CYP) activity.[2–4] They also confirm the results observed in our recent study published in the same journal in patients hospitalized for SARS-CoV-2 infection.[5] We have shown that inflammation induced by SARS-CoV-2 infection has a differential impact on CYP450s. As confirmed by Le Carpentier *et al.*, we have shown that the metabolism of midazolam, a CYP3A4/5 substrate, is decreased in patients hospitalized with SARS-CoV-2 infection and is inversely associated with CRP levels. The two publications reached the same conclusions despite two distinct features in the methodology: (i) the study by Le Carpentier *et al.* was conducted in the context of midazolam infusion in an intensive care unit, whereas our study used a cocktail approach in patients hospitalized with moderate to severe SARS-CoV-2 infection; (ii) a population pharmacokinetic (PopPK) modeling approach was used by Le Carpentier *et al.* allowing a detailed pharmacokinetic (PK) analysis of midazolam, including CRP as a covariate, whereas a multiple linear regression model was used in our study. Regarding the question of the association of other inflammatory markers with CYP activities raised by the authors, this issue was also addressed in our recent paper: the change in activity of some CYPs observed during SARS-CoV-2 infection was associated with IL-6 levels (CYP1A2 and CYP2C9), and TNF-α levels (CYP2D6). Clinicians should be aware of the marked reduction in CYP3A4/5 activity in patients with COVID-19, which could have a lasting impact on the PKs of many drugs used to treat acute SARS-CoV-2 infection or as routine patients' therapy.

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CONFLICT OF INTEREST

The authors declared no competing interests for this work.

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