Dear Editor,

We thank Manciulli and colleagues for their comment on the recently released guidelines from the Italian Society of Anti-Infective Therapy (SITA), the Italian Society of Pulmonology (SIP)

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Therapy (SITA) and the Italian Society of Pulmonology (SIP) on the clinical management of adult patients with coronavirus disease 2019 (COVID-19) outside intensive care units [1, 2]. In their comment, Manciulli and colleagues highlight that, while in the guidelines there is a recommendation against the use of neutralizing monoclonal antibodies in inpatients with COVID-19 (pending results of ongoing trials), the Italian Medicine Agency (AIFA) has recently allowed the use of casirivimab/imdevimab at high dosage in hospitalized seronegative patients with COVID-19 [3]. This apparent discrepancy is mostly related to the fact that the randomized trial (currently available as a non-peer-reviewed pre-print manuscript [4]) supporting the AIFA decision became available only very recently, after the last literature update dictating guidelines development. The possibility of novel evidence becoming available after the release of the guidelines was not unexpected. Indeed, a novel rigorous literature search supporting a predefined update of the current guidelines is about to start in November 2021, as stated in the guideline methods [1]. Nonetheless, it is certainly true that novel evidence cannot be ignored. For this reason, pending the predefined update of the current guidelines, we invite Italian physicians to follow the most recent regulatory document, i.e., the current AIFA recommendations on the use of neutralizing monoclonal antibodies in non-hospitalized and hospitalized patients with COVID-19. However, an important point of caution is that neither the certainty of evidence nor the strength for this recommendation can be reliably defined without the proper methodology. Indeed, the formulation of the final, updated SITA and SIP recommendations on the use of neutralizing monoclonal antibodies (both in inpatients and in outpatients and both for intravenous and for other available formulations) will be provided after following the same rigorous systematic steps that were taken during the preparation of the first released document. This is necessary to guarantee the

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required high-quality standards for guideline development.

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**Compliance with Ethics Guidelines.** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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