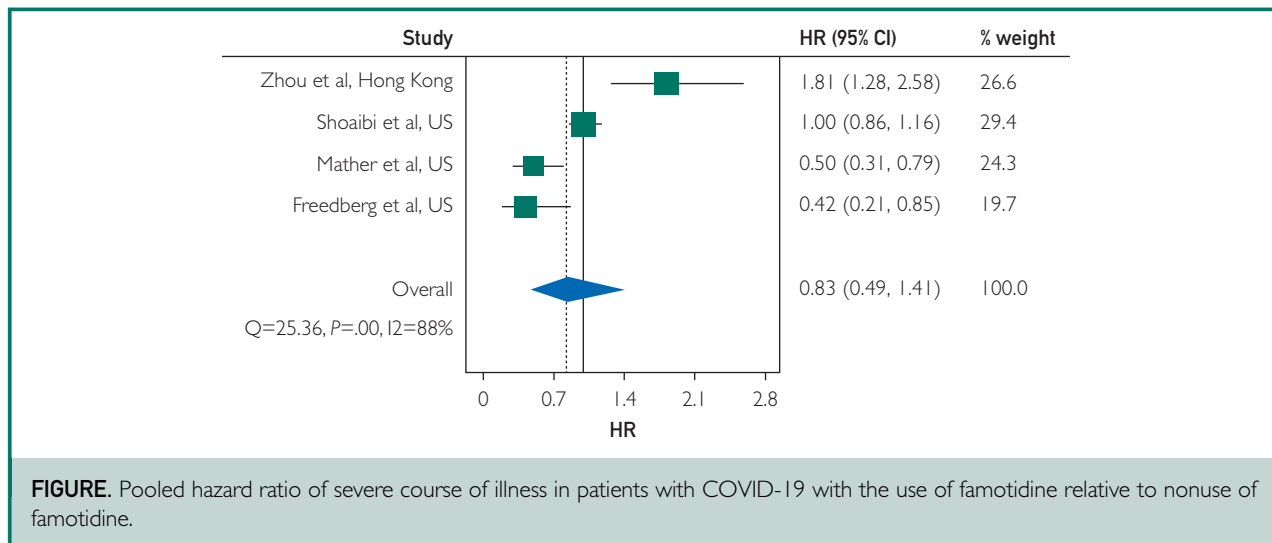**FIGURE.** Pooled hazard ratio of severe course of illness in patients with COVID-19 with the use of famotidine relative to nonuse of famotidine.

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In Reply—Use of Famotidine and Risk of Severe Course of Illness in Patients With COVID-19: A Meta-analysis

To The Editor: Kow and colleagues' interest in our recent letter to the editor[1] regarding the potential for famotidine in COVID-19 infection was much appreciated. Obviously, their meta-analysis is small and probably not adequately powered but still suggested 37% and 7% reductions in severe disease in the general and adjusted analyses, respectively: obviously, with wide confidence intervals that were not close to statistical significance. A large-scale randomized study that was adequately powered, preferably with famotidine, started early in COVID-19, would be required to fully determine the full potential of the benefits of famotidine in COVID-19; this type of study is likely not coming in this pandemic. However, their meta-analysis does not provide much reason for concern regarding significant harms or risks with famotidine in COVID-19.

At present, many clinicians are recommending not only famotidine but several other nonprescription fairly harmless therapies including vitamins C and D, zinc, melatonin, and H1 antihistamine agents for outpatient therapy in COVID -19, all with various degrees of evidence.[2] At present, an old generic prescription medication, colchicine, typically used for gout,[3] but also for pericarditis, is now used with considerable evidence for coronary artery disease.[3] Colchicine is now being considered in COVID-19, originally based on the Greek Study in the Effects of Colchicine in Covid-19 Complications Prevention (GREECO-19) study[4,5] and now with considerably more evidence in the recently released Colchicine Coronavirus SARS-CoV2

(COLCORONA) trial.[6] In this latter major trial, 4159 patients with polymerase chain reaction-confirmed COVID-19, colchicine (0.5 mg twice daily for 3 days, then once daily for 27 days) reduced the primary end point of hospitalization and death significantly by 25%, including significant reductions in hospitalization by 25%, and trends for mechanical ventilation and death (−50% and −44%, respectively). Certainly, evidence for various therapies in COVID-19 continues to evolve rapidly.[7,8]

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Safety of Convalescent Plasma Transfusion

To the Editor: We read with interest the Letter to the Editor by Juskewitch and colleagues,[1] recently published in *Mayo Clinic Proceedings*, in which the investigators observed an unusually high rate (16/157 [10.1%]) of positivity in screens for human leukocyte antigen antibody (HLA-Ab), implicated in transfusion-related acute lung injury (TRALI), in donors of coronavirus disease 2019 (COVID-19) convalescent plasma (CCP). As 5 of them (5/157 [3.1%]) were male donors without a previous known risk factor for the development of HLA-Ab, the authors raised concerns about the safety of CCP. In this regard, we would like to share our experience with the collection and transfusion of CCP at the city hospital of Mantova, Italy. Between March 15, 2020, and February 15, 2021, 516 CCP units were collected from 511 donors (451 men and 60 women; median age, 44.5 years; range, 18-65 years) who had recovered from COVID-19. According to the indications from the Italian National Blood Center, a mandatory condition for donor eligibility was being a man or a nulliparous woman with a negative history of blood component transfusion.[2] All these CCP units were transfused to 296 COVID-19 patients (208 men and 88 women; median age, 70.2 years; range, 29-89 years). Of them, 117 patients received 1 unit; 142 patients, 2 units; 33 patients, 3 units; and 4 patients, 4 units. Adverse reactions to CCP transfusion were recorded in a computer database using the national hemovigilance system of the transfusional network organized by the Italian National Blood Center. Overall, 7 (1.3%) adverse reactions were recorded. All cases were mild allergic reactions characterized by pruritus or rash, which rapidly faded with slowing of the CCP transfusion and after treatment with intravenous administration of antihistamine agents. In no case was it necessary to stop the plasma transfusion. No cases of TRALI occurred. Our data, which document the low rate of adverse reactions to hyperimmune plasma transfusion, are in agreement with the larger experience from the US Food and Drug Administration Expanded Access Program, which showed a low rate (<1%) of severe adverse reactions among 20,000 hospitalized COVID-19 patients transfused with CCP.[3] In conclusion, we agree with Juskewitch and colleagues[1] on the need for further studies aimed at elucidating the role of HLA-Ab in the onset of TRALI associated with CCP transfusion. Nevertheless, on the basis of the real-life data from our study and other studies, we believe that such risk is very low if not negligible.

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