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Convalescent Plasma for Outpatients with Covid-19. Reply

Frederick K. Korley, M.D., Ph.D.,
University of Michigan Ann Arbor, MI

Valerie Durkalski-Mauldin, Ph.D.,
Medical University of South Carolina Charleston, SC

Clifton W. Callaway, M.D., Ph.D.
University of Pittsburgh Pittsburgh, PA

THE AUTHORS REPLY:

We acknowledge the limitations of our study raised by Fisher and Malnick and by Schulz. In response to Fisher and Malnick, we chose to include patients within 1 week after Covid-19 symptom onset in order to target a time period during which endogenous antibodies to SARS-CoV-2 are less likely to be present[1] and Covid-19 symptoms, which typically appear in the second week of illness, are not common.[2] Observational data suggesting an association between better outcomes and treatment with convalescent plasma within 3 days after symptom onset are intriguing, but we did not observe differential treatment effects in the 246 patients who were enrolled within 3 days after symptom onset (see Fig. 2 in our article, available at NEJM.org).

Second, we chose a primary outcome of progression of Covid-19 from an illness that did not require hospital admission to any illness that did require unscheduled medical attention or to death without hospitalization. This outcome is patient-centered, is relevant to health care utilization, and was designed to prevent the failure to notice any of the protean effects of Covid-19. The components of this primary outcome in our population were predominately symptoms related to a viral illness (see Fig. S4 and Table S4 in the Supplementary Appendix of the article, available at NEJM.org). Prespecified secondary outcomes included ratings on an eight-category ordinal scale of illness (see Fig. 3 in the article).

In response to Schulz, we used risk factors for severe Covid-19 illness as defined by the Centers for Disease Control and Prevention. Severe illness included but was not limited to death.[3] These patient characteristics do imply a risk for hospitalization, as evidenced by the 158 of 511 patients (30.9%) who reached the primary outcome — a rate much higher than the rates in other trials involving outpatients with Covid-19.[4]

We agree that more study is required regarding the treatment of immunodeficient patients, including those with cancer. There remain many questions regarding dosing,

callawaycw@upmc.edu .

Since publication of their article, the authors report no further potential conflict of interest.

pharmacokinetics, and patient selection that cannot be addressed in a single trial investigating the use of convalescent plasma in one particular outpatient population with Covid-19.

Finally, we are in the process of analyzing both baseline and subsequent antibody levels in the trial participants over 30 days. We hope that the trajectories of the antibody responses in individual patients will provide insight into disease progression and will help in the design of future studies.

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