## Randomized Controlled Trial of convalescent plasma in COVID-19:

## Negative but Inconclusive

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Arturo Casadevall, MD, PhD Department of Molecular Microbiology and Immunology Johns Hopkins School of Public Health 615 N. Wolfe Street Room E5132 Baltimore, Maryland 21205 acasade1@jhu.edu To the Editor:

Simonovich et al [1] concluded that convalescent plasma (CP) is ineffective in severe COVID-19. Even though double-blinded and randomized, the cohorts were unbalanced: the CP group had more males (70.6% vs 61%), elderly >80 yrs (11.8% vs 7.6%), chronic obstructive pulmonary disease (10% vs 1.9%), higher ferritin (939 vs 645 ng/ml), worse oxygenation (26.53% vs 21.9%) and more intensive care (29.4% vs. 23.8%) than the control group, all associated with worse prognosis [2] [3][4, 5] [6]. The control group also received more tocilizumab (7.6% vs 2.6%; p:0.04) and corticosteroids (96.1% vs. 91.6%).

Randomization in small studies can produce unequal cohorts, which may have inadvertently created a sicker CP cohort. This combined with late administration in infection as evident from SARS-CoV-2 antibodies on >50% of patients in both groups, could explain the negative results. These results contrast to another Argentinean study that reported CP efficacy in preventing severe disease (RR: 0.40; p: 0.007) in elderly patients when given within the 3 days of symptoms [7]. Hence, we caution about conclusions and generalizations from this study.

## **Bibliography**

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