

April 23, 2022

Dr Tedros Adhanom Ghebreyesus
Director
World Health Organization
Geneva, Switzerland

Dear Dr Tedros Adhanom Ghebreyesus,

We write to request that the WHO update its COVID-19 convalescent plasma (CCP) recommendations, last issued on December 7, 2021, that recommended against its use in early disease stages. A prior statement by the U.S. COVID-19 Convalescent Plasma Project leadership argued that this recommendation was misguided based on the knowledge available at the time (1). WHO recommendations are based largely on the analysis of randomized controlled trials published early in the pandemic that focused on hospitalized patients with late-stage disease. As we have noted in a comprehensive analysis (2), the majority of these RCTs used CCP too late in the course of disease to affect outcome.

Since December 2021, additional powerful evidence has been published showing that CCP is effective when used early in the course of disease (3). [Both the Infectious Disease Society of America](#) and the [Association for the Advancement of Blood & Biotherapies \(AABB\)](#) now recommend the early use of CCP in certain COVID-19 patient populations. The totality of current evidence indicates that CCP administration with units having a high concentration of antibodies to SARS-CoV-2 reduces the likelihood of hospitalization and reduces mortality if administered to out-patients early in the course of disease.

The efficacy of CCP is comparable, or even superior, to that seen in registration trials for monoclonal antibodies and small-chemical antivirals when infused within the first five days of symptoms. CCP reduces the rate of hospitalization by about 80% in immunocompetent outpatients at risk of disease progression (3). Furthermore, CCP is finding major use in immunosuppressed patients who often cannot make adequate antibody responses following vaccination or after infection (4, 5).

While antiviral therapies have been available in affluent countries, low- and middle-income countries often lack the financial resources to order expensive monoclonal antibodies and antiviral drugs to treat COVID-19. However, these countries do have the capacity to produce CCP. Manufacturing CCP is nowadays easier than ever thanks to the availability of vaccinated convalescents among regular donors: in them, vaccination boosts neutralizing antibody titers and expands their cross-reactivity against multiple variants of concern. The safety of CCP has been confirmed in hundreds of thousands of patients (6).

It is important also to note that only a few monoclonal antibodies retain their effectiveness against newly mutated strains, such as the currently circulating variant of concern, BA.2. We are confident that if you review the information now publicly available you will amend WHO recommendations to support CCP use in certain patient populations, as previously done by both the IDSA and AABB. We believe this step should be taken URGENTLY to encourage countries to make CCP available to their citizens, a step with the potential to save many lives.

Sincerely yours,

The US Convalescent Plasma Project Leadership team (ccpp19.org)

Arturo Casadevall MD, PhD, Johns Hopkins School of Public Health, USA

Brenda Grossman MD, Washington University, USA

Jeffrey Henderson MD, PhD. Washington University, USA
Michael Joyner MD, Mayo Clinic, USA
Nigel Paneth MD, Michigan State University, USA
Liise-anne Pirofski MD, Albert Einstein College of Medicine, USA
Shmuel Shoham MD, Johns Hopkins School of Medicine, USA

Other signatories

Daniele Focosi MD, PhD, North-Western Tuscany Blood Bank, Italy
Neil Gaffin MD, Valley Health System, USA
Dok Mo MD, Bandung, Indonesia
Jimena Prieto MD, Programa Nacional de Trasplante Hepático, Uruguay

.....

1. Paneth N, Casadevall A, Pirofski LA, Henderson JP, Grossman BJ, Shoham S, and Joyner MJ. WHO covid-19 drugs guideline: reconsider using convalescent plasma. *Bmj*. 2022;376(o295).
2. Focosi D, Franchini M, Pirofski LA, Burnouf T, Paneth N, Joyner MJ, and Casadevall A. COVID-19 Convalescent Plasma and Clinical Trials: Understanding Conflicting Outcomes. *Clin Microbiol Rev*. 2022:e0020021.
3. Sullivan DJ, Gebo KA, Shoham S, Bloch EM, Lau B, Shenoy AG, Mosnaim GS, Gniadek TJ, Fukuta Y, Patel B, et al. Early Outpatient Treatment for Covid-19 with Convalescent Plasma. *The New England journal of medicine*. 2022.
4. Focosi D, and Franchini M. Potential use of convalescent plasma for SARS-CoV-2 prophylaxis and treatment in immunocompromised and vulnerable populations. *Expert review of vaccines*. 2021:1-8.
5. Thompson MA, Henderson JP, Shah PK, Rubinstein SM, Joyner MJ, Choueiri TK, Flora DB, Griffiths EA, Gulati AP, Hwang C, et al. Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19. *JAMA oncology*. 2021;7(8):1167-75.
6. Senefeld JW, Johnson PW, Kunze KL, van Helmond N, Klassen SA, Wiggins CC, Bruno KA, Golafshar MA, Petersen MM, Buras MR, et al. Program and patient characteristics for the United States Expanded Access Program to COVID-19 convalescent plasma. *medRxiv*. 2021:2021.04.08.21255115.