Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Convalescent plasma in patients hospitalised with COVID-19

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As the COVID-19 pandemic continues, researchers continue to search for effective treatments. The often unpredictable disease course of COVID-19 creates a substantial challenge for clinical researchers when identifying ideal patient populations who might benefit from investigational interventions. One of the first promising therapeutics considered was convalescent plasma. Several retrospective observational studies in 2020 suggested a beneficial role of convalescent plasma for patients hospitalised with severe COVID-19.[1–3] Following these initial reports, a series of peer-reviewed randomised trials did not confirm the positive findings.[4–6] The absence of efficacy of convalescent plasma is now reinforced by the results from the RECOVERY Collaborative Group,[7] published in *The Lancet*, in which 5795 patients received convalescent plasma plus usual care and 5763 received usual care alone in a randomised, open-label study done in 177 National Health Service hospital organisations in the UK. Of the 11 558 randomly assigned patients, 4128 (36%) were women and the mean age was 63·5 (SD 14·7) years. Halted prematurely by an independent data monitoring committee, no significant differences between groups in 28-day mortality were observed. This adds to the growing number of convalescent plasma trials that were stopped for futility, including CONCOR-1 (NCT04348656) and REMAP-CAP (NCT02735707).[8,9]

Reuters/Arnd Wiegmann

The RECOVERY study[7] combines a thoughtful design with a thorough analysis in the setting of current standard practices and realistic samplings of patients hospitalised with COVID-19. Primary limitations of the study include its UK only setting, poor ethnic diversity, and a long median time from symptom onset to randomisation of 9 (IQR 6–12) days. The study succeeds in capturing key features previously missed in earlier trials with convalescent plasma. Of note, the large number of study participants reassures the validity of the findings. In addition to its study size, the trial rightfully focused away from patients requiring mechanical ventilation (617 [5%] of all randomly assigned participants) who would not likely benefit from an antibody-based treatment. The enrolled participants accurately reflected international standards of care, with 10 681 (92%) patients receiving corticosteroids. After enrolment and random assignment, selected participants received two units of convalescent plasma. Each convalescent plasma unit required a sample to cutoff ratio of 6·0 or more on the EUROIMMUN IgG ELISA test targeting the spike glycoprotein (PerkinElmer, London, UK). By US Food and Drug Administration standards,[10] all of these units would be regarded as high-titre units (EUROIMMUN sample to cutoff ratio of ≥3·5; Convalescent Plasma Emergency Use Authorization Letter of Authorization March 9, 2021).

The primary outcome was all-cause mortality 28 days after randomisation, and there was no evidence that convalescent plasma provided any benefits over and above usual care. Additionally, no significant effect was observed on the proportion of patients discharged from hospital within 28 days. An extensive subgroup analysis did not identify a unique cohort that would benefit from receiving convalescent plasma. Patients with shorter durations of symptoms shared similar outcomes as those later in their disease course. There was a slight rate ratio reduction of 0·90 (95% CI 0·82–0·97) for invasive mechanical ventilation or death in the study population with a negative SARS-CoV-2 antibody test; however, this reduction was not significantly different when compared with the SARS-CoV-2 antibody test positive and unknown subgroups. The data collection period occurred between May 28, 2020, and Jan 15, 2021,

and the emergence of the B.1.1.7 variant in late 2020 was also considered. A pre-Dec 1, 2020, versus post-Dec 1, 2020, subanalysis showed no differences to suggest that the B.1.1.7 variant disrupted the study's findings.

Despite the many challenges of doing rigorous clinical research during the COVID-19 pandemic, the RECOVERY Collaborative Group has contributed valuable conclusions against the use of convalescent plasma for patients hospitalised with COVID-19. Special populations, such as patients with impaired humoral immunity, who were not actively considered in this study, might still benefit from convalescent plasma when admitted.[11] Convalescent plasma might also find a therapeutic role in an ambulatory setting for mild-to-moderate COVID-19, as supported by Libster and colleagues;[12] however, the clinical trial of COVID-19 convalescent plasma of outpatients (C3PO; NCT04355767) determined that this cohort was unlikely to benefit.[13] Future ambulatory trials with convalescent plasma might need to be matched against monoclonal antibody therapies or hyperimmune immunoglobulin, and eligibility criteria will need to tightly define the population most likely to benefit. The amount of effort invested in each convalescent plasma transfusion, from donor to blood bank to medical team to patient, deserves an equally great amount of consideration of whether the transfusion will provide any benefit. Current and future studies are exploring the next class of COVID-19 therapeutics, including small-molecule antivirals, next-generation monoclonal and polyclonal antibody therapies, and immunomodulatory agents.

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*Sean T H Liu, *Judith A Aberg*
judith.aberg@mssm.edu

Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA

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Targeting IL-6 in patients at high cardiovascular risk

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The understanding that atherosclerosis is a chronic inflammatory disorder mediated through both adaptive and innate immunity has led to the hypothesis that anti-cytokine therapies targeting interleukin signalling pathways could serve as adjuncts to lipid lowering in the prevention and treatment of cardiovascular disease.[1] The Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS) showed that targeting interleukin (IL)-1β reduced cardiovascular event rates without lowering lipids or blood pressure.[2] The magnitude of this effect was directly associated with the reduction in IL-6 and the downstream clinical biomarker high-sensitivity C-reactive protein (CRP). CANTOS included a subgroup of 1875 patients with chronic kidney disease (estimated glomerular filtration rate [eGFR] <60 mL/min per 1·73 m^2). In this subgroup