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.

independently correlated with low IgG(S-RBD) titres in multivariable analysis, whereas the correlation with the time interval between HSCT and vaccination was lost. With a median follow-up of 84 days (range 44–121 [IQR 65–110]) after the first vaccination dose, we did not observe any COVID-19 infection in this cohort.

In this first evaluation of immunogenicity in allogeneic HSCT recipients after two vaccine doses, we observed overall frequent and high levels of humoral responses, which contrasts with recent observations in solid organ transplant recipients who are receiving very long-term pharmacological immunosuppression.[4] We identified lymphocyte count as well as recent pharmacological immunosuppression, rather than the sole timing of vaccination after HSCT, as determinants of humoral response. Our findings support the large scale vaccination of allogeneic HSCT recipients, although additional multicentre and long-term studies are needed to specify the level of immunological protection against infection, also taking into account the effect of a third vaccine dose in non-responding patients.

We declare no competing interests.

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Tocilizumab in COVID-19 therapy: who benefits, and how?

The randomised controlled RECOVERY trial[1] has met its primary endpoint of reduced 28-day mortality. We congratulate the RECOVERY Collaborative Group for this excellent study. However, the mortality at day 28 was up to 31% in the tocilizumab group and was higher than the results of other published randomised controlled trials.[2] The pathophysiology underlying COVID-19 is characterised by SARS-CoV-2 viral infection-induced inflammatory response, cell death, and microvascular thrombosis. Thrombosis appears to be common in patients with COVID-19 pneumonia and could also be responsible for multiorgan failure in patients who are critically ill.[3] Larger studies have shown that patients with COVID-19 are at increased risk of thrombosis and that 29·4% of patients in the intensive care unit had a thrombotic event (13·6% venous and 18·6% arterial).[4] Furthermore, the thrombotic event is independently associated with mortality of COVID-19 patients.[4]

ClinicalTrials.gov records thrombotic events including acute pulmonary embolism, deep vein thrombosis, ischaemic stroke, myocardial infarction, or systemic arterial embolism as the prespecified outcome of this study protocol. However, the RECOVERY Collaborative Group omitted such important outcomes from the published results without any clear explanation.

There is clinical evidence to suggest tocilizumab therapy in patients with COVID-19 may be associated with thrombotic events.[5] To better analyse the efficacy and safety of tocilizumab, the RECOVERY Collaborative Group should specify the number of thrombotic or thromboembolic events observed in their study and specifically detail the proportion of patients receiving therapeutic anticoagulation in both groups. These results will better inform clinical practice on the use of tocilizumab for patients with COVID-19.

CY is a former postdoctoral fellow at the University Health Network. We declare no competing interests.

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Steve Parsons/PA Wire/Bloomberg via Getty Images

The RECOVERY Collaborative Group reported statistically significant improvement in survival of patients with COVID-19 who were receiving tocilizumab interleukin (IL)-6 inhibitor, albeit with very modest reduction of mortality (31% *vs* 35% with usual care, p=0·0028).[1] This result adds to a number of studies with tocilizumab and other IL-6 antagonists, such as sarilumab, which showed only minor, or no, reduction in mortality.[2] Given that IL-6 is associated with COVID-19 severity and mortality,[3] the question arises as to why IL-6 antagonist therapy does not substantially improve survival.

In April, 2021, we showed that IL-6 serum concentrations are indeed associated with COVID-19 severity (appendix); however, a better classification of severity is obtained when IL-6 is combined with other cytokine concentrations.[4] Moreover, within each respiratory severity group, IL-6 is not significantly associated with mortality (appendix). It is rather distinct combinations of interferon α, inteferon β, IL-10, and tumour necrosis

See **Online** for appendix

factor α that are better predictors of mortality in different severity groups.[4]

Nevertheless, mortality in the low IL-6 group of patients is significantly lower than in the high IL-6 group of patients (appendix), suggesting that IL-6 inhibitors should be given only to patients with high IL-6. Indeed, a retrospective analysis of tocilizumab therapy as a function of baseline IL-6 concentrations showed a large reduction in mortality (from 36% to 16%) in patients with high-baseline IL-6, but no reduction in mortality in low-baseline IL-6 patients.[5]

See Online for appendix

In conclusion, clinical trials of IL-6 antagonist therapy, such as RECOVERY[1] and sarilumab COVID-19 global studies,[2] should consider reanalysis of their results as a function of IL-6 baseline concentrations. More generally, clinical trials of personalised precision medicine, based on cytokine profiling, are needed for optimisation of COVID-19 therapy.

For the **Series on progress in maternal and child undernutrition** see https://www.thelancet.com/series/maternal-child-undernutrition-progress

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Authors' reply

We thank Chengliang Yang and Hedi Zhao for their interest in the thrombotic event rate in the RECOVERY trial of tocilizumab in patients hospitalised with COVID-19.[1] Data on thrombotic events were only collected on follow-up forms from Nov 1, 2020, so these data are only available for about 60% of participants. Nevertheless, we observed no difference in the thrombotic event rate between patients allocated to tocilizumab or usual care alone (appendix).

Avidan Neumann and colleagues have suggested a post-hoc analysis of outcomes stratified by baseline levels of inflammatory biomarkers, to examine the hypothesis that a larger therapeutic response to interleukin (IL)-6 inhibition might be observed in patients with higher levels of inflammatory biomarkers. In the RECOVERY trial,[1] all patients included in the tocilizumab comparison were required to have a C-reactive protein (CRP) concentration of 75 mg/L or more; therefore, the trial already restricted the comparison with a patient subgroup selected on a biomarker. Although we did not collect data on baseline IL-6 concentrations, CRP data were collected because CRP is associated with IL-6 concentrations and clinical severity, and is globally a more affordable and available biomarker than IL-6.[2] In a post-hoc analysis of the primary outcome of 28-day mortality based on approximate tertiles of CRP there was no evidence of heterogeneity of effect by baseline CRP concentration of 75 mg/L or more (p=0·30; appendix). These data do not, therefore, support the hypothesis of restricting treatment with tocilizumab to those patients with the highest levels of CRP or other biomarkers of inflammation. On the contrary, these data raise the question of whether even more COVID-19 patients could benefit from IL-6 inhibition if a lower threshold (CRP <75 mg/L) were used to initiate treatment.

We declare no competing interests.

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The nutrition agenda must include tobacco control

The Lancet's Series on progress in maternal and child undernutrition reminds us that malnutrition and stunting, and the double burden of obesity and malnutrition, remain important priorities for achieving Sustainable Development Goal 3 and other goals for child health. However, although recognising the importance of the environment and commercial determinants of food availability, the nutrition agenda continues to ignore the importance of tobacco control in achieving nutritional goals.

Adult tobacco users consume significant calorie equivalents, and adult smoking is associated with hunger and food insecurity for household children and adults in high-income[1,2] and low-income[3,4] countries. Second-hand smoke exposure is associated with overweight and obesity, and the inflammatory effects of smoke can cause metabolic syndrome, dyslipidaemia, insulin resistance and diabetes, and premature atherosclerotic heart disease.[5] Strong evidence-based interventions for comprehensive tobacco control are described in the Tobacco Free Initiative MPOWER package of interventions,[6] which have been recognised and endorsed by WHO and the 22 other UN agencies that participate in the UN Interagency Task Force on Tobacco.