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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 trial¹ 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.

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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 , interferon β , IL-10, and tumour necrosis



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See Online for appendix