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.

3 Wynants L, Van Calster B, Collins GS, et al. Prediction models for diagnosis and prognosis of COVID-19 infection: systematic review and critical appraisal. *BMJ* 2020; **369:** m1328.
4 Calfee CS, Delucchi KL, Sinha P, et al. Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. *Lancet Respir Med* 2018; **6:** 691–98.

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In *The Lancet Rheumatology*, Giacomo De Luca and colleagues[1] examined whether mavrilimumab added to standard care could improve the clinical outcomes in patients with COVID-19 pneumonia and systemic hyperinflammation in a single-centre prospective cohort study. They compared 13 patients treated with mavrilimumab to 26 patients who received standard care. The analysis showed earlier clinical improvement in the intervention group than in the control group. However, the power of study was low due to the small sample size, and no statistical difference in mortality was found between the two groups (no patients died in the mavrilimumab group *vs* seven [27%] patients in the control group; p=0·086). The challenges of doing clinical studies to find safe and effective therapies during the COVID-19 pandemic are understandable, with shortfalls of adequate actions against the unknown disease and its complication in resource-limited conditions and given concerns over a potentially high case–fatality rates. However, as Cheung and colleagues caution,[2] underpowered studies that are susceptible to type II error could discourage clinicians from using potentially effective treatments against COVID-19 and lead to premature rejection of promising drugs.

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Although a prospective cohort, De Luca and colleagues' study[1] was done at a single centre, and patients were matched with a control group. As they mentioned in their limitations section, the absence of a pre-established randomisation process can introduce risks for selection bias. Although the distribution of demographic variables for both groups indicated no significant differences, one should note that this lack of difference might be due to low sample size, because a small sample size is more likely to show no difference according to type II error. In this case, the authors could use multivariate analysis (including a Cox regression model) to control for the potential confounders (eg, the predominance of male participants and longer fever duration in the intervention group than in the control group).

In summary, no strong conclusions about the effects of mavrilimumab in COVID-19 can be made until an appropriately powered trial has been done with appropriate statistical analysis to avoid potential bias.

We declare no competing interests.

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1 De Luca G, Cavalli G, Campochiaro C, et al. GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study. *Lancet Rheumatol* 2020; **2:** e465–73.
2 Cheung MP, Lee TC, Tan DHS, et al. Generating randomized trial evidence to optimize treatment in the COVID-19 pandemic. *CMAJ* 2020; **192:** 405–07.

Authors' reply

We thank Mohamad Amin Pourhoseingholi and colleagues and Manish Soneja and colleagues for their interest in our Article.[1] As we stated in our manuscript, we agree that the small number of enrolled patients does not allow us to draw definitive conclusions on the effect of mavrilimumab on mortality in patients with COVID-19, and that randomised controlled trials are needed to unequivocally assess the efficacy and safety of this therapeutic strategy. However, we feel that the clinical data on clinical improvement emerging even in our small cohort support the strength of our results. Indeed, in our single-centre, prospective cohort study, we showed that single-dose mavrilimumab, administered in 13 patients with severe COVID-19 pneumonia and hyperinflammation, was associated with significantly greater and faster clinical improvement than standard management alone in a cohort of 26 patients.

As we stated in our Article, we are aware that the study design and the absence of a pre-established randomisation process can introduce risks for selection bias, treatment bias, and hence type II error. The same study design (prospective cohort study) has been adopted in many recent anti-cytokine therapies studies in this novel and unfamiliar clinical scenario[2–4] and these studies have contributed to the development of subsequent randomised controlled trials, most of which are still ongoing.

Additionally, in a pre-planned analysis, we used a Cox proportional-hazards model with treatment and a 7-point scale of clinical status at baseline as covariates to identify whether these variables were mutually independent factors associated with time to improvement in clinical status, and we found that both variables were independent predictors of clinical improvement at multivariate analysis (treatment: relative risk 5·84 [95% CI 2·5–13·6; p<0·001]; clinical status: 2·9 [1·3–6·5; p=0·011]). These data were not included in the Article because the final statistical model was considered appropriate for a non-randomised setting.

We agree that our definition of hyperinflammation might be considered somehow arbitrary, but we believe that any cut-off determined in pioneering studies is unavoidably arbitrary, and this was the case while dealing with the truly unprecedented condition that is COVID-19 pneumonia. Furthermore, similar cut-off values for C-reactive protein (CRP), ferritin, interleukin (IL)-6, and lactate dehydrogenase