LETTER

REPLY TO WANG ET AL.:

Tocilizumab treatment should be used in a timely manner, at suitable dose, and in suitable patients

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We thank Wang et al. (1) for their Letter, and we understand their concern about the uncertain effectiveness of tocilizumab treatment in COVID-19 patients. Tocilizumab is not a magical therapeutic that can save all of the lives of COVID-19 patients. However, if tocilizumab is used properly, it may reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia. After our exploration, this tocilizumab treatment and related scientific strategy against inflammatory cytokines have gained wide attention. Until now, there have been more than 60 clinical trials related with tocilizumab toward COVID-19 worldwide, and most of them are still underway recruiting patients. Many clinical research groups have confirmed that the response to tocilizumab was rapid, sustained, and associated with significant reduction in the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia (2–6). For example, a large-scale retrospective cohort study that admitted 1,351 patients from Italy showed significantly decreased mortality in patients treated with tocilizumab compared with patients in the standard care group (7), confirming the effectiveness of tocilizumab treatment, whether administered intravenously or subcutaneously.

In our experiences of tocilizumab treatment toward COVID-19, timely and adequate intervention is very critical. We recommend that use of tocilizumab in conditions when patients are moderate or progressing to severe cases. For critical patients who have a persistent high level of IL-6 for a long time, or even have already had extensive and severe irreversible damage to the lungs and even other organ failure, tocilizumab intervention that begins at this stage can hardly reverse the situation. Furthermore, the age, baseline disease, and other medicine or treatment accompanied with tocilizumab should also be evaluated. In our study in PNAS (8), we find that the IL-6 levels would be temporarily increased after tocilizumab, for its receptors have been blocked by tocilizumab. Similar conditions can be observed in another multicenter study (9).

For whether tocilizumab treatment has the high risk of serious infections, there are sufficient studies in this treatment of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome. No significant higher risk of serious infection has been observed in these tocilizumab treatments (10). On the basis of safety and effectiveness, the US Food and Drug Administration approved tocilizumab for the treatment of severe or life-threatening CAR T cell-induced cytokine release syndrome in adults and in pediatric patients 2 y of age and older. Furthermore, our single-cell analysis of peripheral blood isolated from severe COVID-19 patients before and after tocilizumab treatment showed that the overactivated inflammatory immune response was attenuated after tocilizumab treatment, yet immune cells including $CD8^+$ T cells and plasma B cells still exhibited an intense humoral and cell-mediated antivirus immune response in recovered COVID-19 patients (11), which further suggested that tocilizumab treatment attenuates the inflammation and keeps the antivirus immune response. Other clinical research with COVID-19 patients further indicates that there is no definite infection related to tocilizumab treatment (6, 9).

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In conclusion, although tocilizumab treatment has shown its effectiveness in reducing the risk of invasive mechanical ventilation and the mortality of COVID-19, it still should be used in a timely manner, at suitable dose, and in suitable patients.

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