Comment to "Dexamethasone treatment for COVID-19 is related to increased mortality in hematologic malignancy patients: results from the EPICOVIDEHA Registry"

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Comment to “Dexamethasone treatment for COVID-19 is related to increased mortality in hematologic malignancy patients: results from the EPICOVIDEHA Registry”

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Contributions
GZ initiated and conceptualised the idea. GZ wrote the letter, JL revised the letter.

We appreciate the work reported by Aiello et al. that dexamethasone treatment of SARS-CoV-2 infection is associated with increased mortality in patients with hematologic malignancies. Due to the clear association between inflammatory dysregulation and adverse clinical outcomes, international guidelines unanimously recommend supporting the use of corticosteroids in hospitalized patients with acute respiratory failure from COVID-19 to reduce mortality in such patients. Glucocorticoid therapy reduced neutrophil influx, blocked T cell response, and reduced cytokine storm. However, excessive doses can trigger immunosuppression, which can be fatal, especially in immunosuppressed population. This study by Aiello et al. seems to raise the alarm about whether glucocorticoid therapy should be used in hematologic malignancy patients. Is it true that hematologic malignancy patients do not benefit from glucocorticoid therapy? Here, we highlight some points of the study that deserve attention.

First, although this study included a large number of patients in multiple centers, due to the retrospective nature of the study and the relatively loose inclusion and exclusion criteria, bias may be unavoidable. Significant differences were observed in the subgroups, including age, comorbidities, status of hematologic malignancy control, vaccination rates, variant duration of infection, severity of infection symptoms, proportion of hospitalizations and ICU admissions. The baseline characteristics of the population using dexamethasone were significantly worse, with lower rates of vaccination, more severe symptoms of infection, and higher rates of hospital admission and ICU admission, which were associated with the risk of death and poor prognosis. In addition, the study was non-randomized and non-interventional, treatment was decided by the attending physician, and based on experience and consensus, glucocorticoid therapy is often used in patients with severe or critically ill COVID-19, especially those with inflammatory storms. This means that people treated with dexamethasone are already critically ill and have a higher risk of death.
Therefore, the causal relationship between dexamethasone and the risk of death in patients needs to be carefully examined. Second, corticosteroids are commonly used to control inflammation in COVID-19 patients. However, there is debate about the optimal timing, dosage, and duration of corticosteroid therapy. While corticosteroids have anti-inflammatory effects, they also suppress the immune response, potentially hindering pathogen clearance and promoting viral replication. Immunocompromised patients are at risk for persistent COVID-19, which is a persistent symptomatic disease with active viral replication. Studies have shown that nearly 14% of patients with hematologic malignancies and SARS-CoV-2 infection still have detectable SARS-CoV-2 viral RNA for 30 days or more. There is persistent viral replication in the lungs, which is associated with accelerated death and secondary bacterial infection. The dosage and duration of dexamethasone use were not described in detail in this study. High doses and long courses of glucocorticoid therapy may be associated with an increased risk of death. High doses and long courses of glucocorticoid therapy inhibit viral clearance, and may lead to high blood sugar, increasing the risk of secondary infections, such as invasive aspergillus. Therefore, it is necessary to identify whether there is persistent SARS-CoV-2 replication in a specific type of immune dysfunction, while carefully considering the dose and timing of corticosteroid use to control inflammation while reducing adverse reactions. This study revealed that patients with hematologic malignancies infected with SARS-CoV-2 have a high risk of death, with a 90-day mortality rate of about 20%. Encouragingly, death was significantly reduced with antiviral therapy, whether combined with dexamethasone. Treatment options include convalescent plasma, monoclonal antibodies and antiviral drugs, both monotherapy and combination therapy. We sincerely hope that the authors will conduct further studies to evaluate the efficacy of several treatments and combinations to provide quality options for these immunocompromised patients. Especially with the emergence of new mutant strains, most monoclonal antibodies may face the possibility of being evaded and ineffective.

REFERENCES
