ICU
MANAGEMENT & PRACTICE

Tocilizumab and COVID-19 Pneumonia

Tocilizumab is a humanised monoclonal antibody that binds human interleukin 6 (IL-6) receptors. It is generally used in inflammatory arthritis, giant cell arteritis and cytokine release syndrome after chimeric antigen receptor T-cell therapy.

Tocilizumab has come under close scrutiny during the COVID-19 pandemic. Early observations from China showed an increased risk of death in COVID-19 patients with elevated IL-6 levels, and tocilizumab was suggested as a possible treatment option. Due to this initial recommendation, the off-label use of the drug increased in COVID-19 patients in the U.S.

However, as more evidence surfaced, both the National Institutes of Health and the Infectious Disease Society of America recommend against the use of tocilizumab except in the context of a clinical trial. Even if some mortality benefit has been observed, there is still insufficient data to make such a recommendation and more reliable data from RCTs of tocilizumab in COVID-19 patients is needed before any such guideline.

So far, the data that have been released do not show any significant benefit from the use of tocilizumab. Study findings from Salvarani et al. (2020) and Hermine et al. (2020), preliminary results from COVACTA and EMPACTA and data from the STOP-COVID study suggest caution when using tocilizumab in COVID-19 patients. None of the tocilizumab trials have reported mortality benefit at 28 or 30 days. Only 2 of these trials have reported outcomes that meet predefined thresholds for clinical efficacy.

Salvarani et al. (RCT-TCZ-COVID-19 Study Group) enrolled patients in Italy with severe COVID-19 who required oxygen by nasal cannula but not ICU care. The goal of the study was to determine the effect of early tocilizumab administration. However, the trial was stopped early because initial analyses did not find any evidence of improvement in primary outcomes.

Hermine et al. (CORIMUNO-19-TOCI-1) enrolled patients in France with moderate or severe COVID-19 pneumonia and oxygen requirement, but these patients did not require high-flow oxygen by nasal cannula, non-invasive ventilation or mechanical ventilation. Findings from this trial suggest that tocilizumab may improve outcomes at 14 days. However, this trial had a very narrow focus, and the significance of these findings is questionable in light of the preliminary results from COVACTA and EMPACTA trials.

The COVACTA study, conducted across North America and Europe, failed to meet predefined efficacy thresholds, and no mortality difference was observed at day 28. Patients who were treated with tocilizumab had reduced length of hospital stay, but all other secondary outcomes were negative. The EMPACTA study, which included patients from minority racial and ethnic groups across the Americas and Africa, showed efficacy in its primary endpoint, reduction of mechanical ventilation or death by day 28 but no difference in mortality was observed and secondary outcomes were negative. Findings from both CORIMUNO-TOCI-1 and EMPACTA suggest that tocilizumab may reduce the need for mechanical ventilation and ICU level care in some patients with severe COVID-19, but things still remain unclear until COVACTA and EMPACTA near completion.

So far, the benefit of tocilizumab in COVID-19 patients remains doubtful and clinical findings do not support routine tocilizumab use in COVID-19. No differences in mortality could be attributed to tocilizumab at day 28 or 30 in any of the trials. Only 2 of the four clinical trials reported evidence of efficacy.

However, there are five other randomised controlled trials of tocilizumab in COVID-19 underway. Findings from these trials can help define its role in COVID-19 management. At this point in time, it is best to wait and see what data emerges from ongoing clinical trials before any recommendation can be made for the use of tocilizumab in COVID-19.

Source: JAMA

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