

Should tocilizumab be used in the treatment of COVID-19?

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This rapid review summarizes the available evidence on the efficacy and safety of tocilizumab in treating patients with COVID-19. This may change as new evidence emerges.

KEY FINDINGS

There is insufficient evidence to conclude on the efficacy and safety of tocilizumab for COVID-19. Although some benefit for patients with severe COVID-19 has been noted, more well-designed prospective clinical trials or observational studies are needed.

- Tocilizumab (Actemra/RoActemra) is an immunosuppressive drug currently used for treating various forms of arthritis.
- As patients with severe COVID-19 pneumonia typically exhibit systemic hyperinflammation and elevated inflammatory markers, tocilizumab has been proposed as one possible treatment for COVID-19 patients.
- There are no available randomized clinical trials yet on tocilizumab for COVID-19. Current available evidence comes from one observational study. Seven (7) clinical trials are ongoing.
- Tocilizumab is recommended by Chinese clinical guidance; no recommendation from WHO
- Current evidence for the efficacy and safety of tocilizumab for COVID-19 is not conclusive.
 Although some benefit for patients with severe COVID-19 has been noted, more well-designed prospective clinical trials or observational studies are needed.

RESULTS

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There are still no completed randomized clinical trials on the topic. Current evidence comes from 1 unpublished case series from China [10], 1 case report from United States [11]. Seven clinical trials are ongoing (3 China, 2 Italy, 1 Denmark, 1 Multi-country).

In a case series involving 21 severe COVID-19 cases in China, tocilizumab resulted in normalization of body temperature (n = 21), lymphocyte counts in 10/19 patients and CRP levels in 17/18 patients on day 5, improvements in lung CT scans and pulmonary function in 19/21 patients. Average time of hospitalization after tocilizumab dose was 13.5 days. No serious adverse events were noted. This study had a high risk of bias.

Tocilizumab has also been tried to treat a 56-year-old ESRD patient with ARDS and septic shock. Final outcomes were not yet available.

Chinese guidelines state that tocilizumab treatment can be tried for patients with extensive lung lesion and severe patients with elevated IL-6 levels, but not for those with active infections (e.g., tuberculosis) [12]. WHO does not have any recommendation regarding tocilizumab use for COVID-19 [13].

CONCLUSION

There is insufficient evidence to conclude on the efficacy and safety of tocilizumab for COVID-19. Although there are some studies demonstrating benefit from using this drug among patients with severe COVID-19, more well-designed prospective clinical trials or observational studies are needed.

Declaration of Conflict of Interest

No conflict of interest

REFERENCES

- 1. Kaly L, Rosner I. Tocilizumab a novel therapy for non-organ-specific autoimmune diseases. Best Pract Res Clin Rheumatol 2012;26:157-65.
- Yokota S, Imagawa T, Mori M, et al. Efficacy and safety of tocilizumab in patients with systemic onset juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled, withdrawal phase III trial. Lancet 2008:371:998-1006.
- 3. Jones G, Ding C. Tocilizumab: a review of its safety and efficacy in rheumatoid arthritis. Clin Med Insights Arthritis Musculoskelet Disord. 2010; 3: 81–89.
- 4. Castagné B, Viprey M, Martin J, Schott A, Cucherat M, Soubrier M. Cardiovascular safety of tocilizumab: a systematic and network meta-analysis. PLoS One. 2019; https://doi.org/10.1371/journal.pone.0220178
- 5. De Benedetti F, Brunner HI, Ruperto N, Kenwright A, Wright S, et al. Randomized trial of tocilizumab in systematic juvenile idiopathic arthritis. N Engl J Med 2012; 367:2385-2395.
- Siddiqi, HK., Mehra, MR. COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal, Journal of Heart and Lung Transplantation 2020. https://doi.org/10.1016/j.healun.2020.03.012
- 7. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Internal Medicine. 2020. doi:10.1001/jamainternmed.2020.0994

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- 8. Zhou F, Yu T, Du R, Fan G, Liu Y, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020. https://doi.org/10.1016/S0140-6736(20)30566-3.
- 9. https://techstartups.com/2020/03/27/breaking-tolicizumab-shown-effective-hydroxychloroquine-treating-coronavirus-patients-doctors-say/
- 10. Xu X, Mingfeng H, Tiantian L, Wei S, Dongsheng W, et al. Effective treatment of severe COVID-19 patients with tocilizumab. 2020. [ChinaXiv:202003.00026] http://chinaxiv.org/abs/202003.00026
- 11. Ferrey AJ, Choi G, Hanna RM, Chang Y, Tantisattamo E, et al. A case of Novel Coronavirus Disease 19 in a chronic hemodialysis patient presenting with gastroenteritis and developing severe pulmonary disease. Am J Nephrol. 2020 Mar 28:1-6. doi: 10.1159/000507417. [Epub ahead of print]
- 12. China National Health Commission. Chinese clinical guidance for COVID-19 pneumonia diagnosis and treatment. 7th edition. 2020 Mar 4. http://kjfy.meetingchina.org/msite/news/show/cn/3337.html
- 13. WHO, Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance. V1.2. 2020, WHO: Geneva.
- 14. Bennardo F, Buffone C, Giudice A. New therapeutic opportunities for COVID-19 patients with Tocilizumab: possible correlation of interleukin-6 receptor inhibitors with osteonecrosis of the jaws. Oral Oncol. 2020 Mar 21:104659. doi: 10.1016/j.oraloncology.2020.104659. [Epub ahead of print]
- 15. Bersanelli M. Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. Immunotherapy. 2020 Mar 26. doi: 10.2217/imt-2020-0067. [Epub ahead of print]

Last Updated: 01/April/20