

Safety Profile of Tocilizumab Use in COVID-19 Critically



III Medical Intensive Care Unit Patients Caleb Brey, PharmD; Hollie Lawrence, PharmD, BCCCP Regions Hospital St. Paul, MN



Background

- Tocilizumab is an interleukin-6 receptor antagonist indicated for immune mediated inflammatory conditions
- Black Box Warning: Serious potentially fatal infections including active tuberculosis, invasive fungal, bacterial, viral, protozoal, and other opportunistic infections
- National initiative to find treatment for COVID-19 pneumonia
- Thought in using tocilizumab is that it will inhibit part of the inflammatory cascade and prevent/limit the inflammation that occurs within the lungs
- Thus limiting progression of illness to the point of requiring mechanical ventilation
- The U.S. Food and Drug Administration has granted tocilizumab emergency use authorization (EUA) for use in COVID-19 based on the results of several studies.
 - RECOVERY Trial
 - No difference in mortality for those that received tocilizumab, did find that patients that received tocilizumab and dexamethasone were more likely to be discharged from the hospital by 28 days
 - EMPACTA Trial
 - Tocilizumab associated with lower combined rate of mechanical ventilation or death
 - COVACTA Trial
 - Tocilizumab use was associated with a shorter time to discharge and shorter ICU length of stay

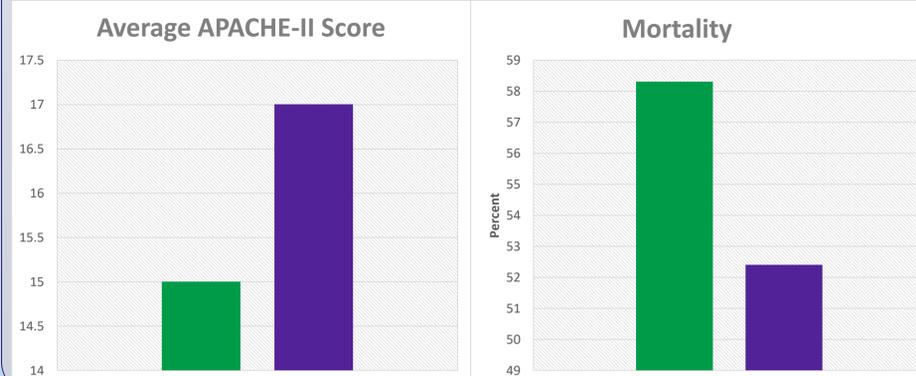
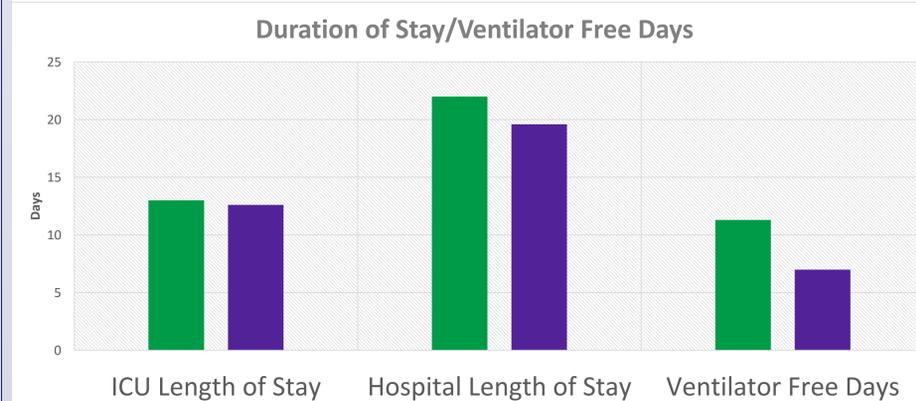
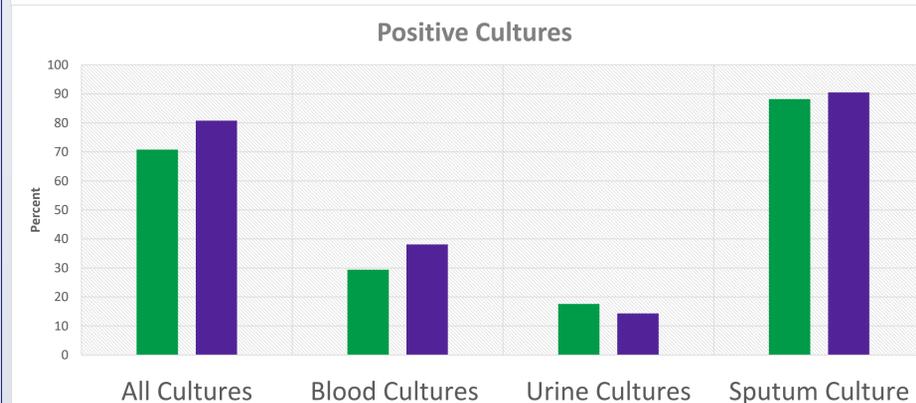
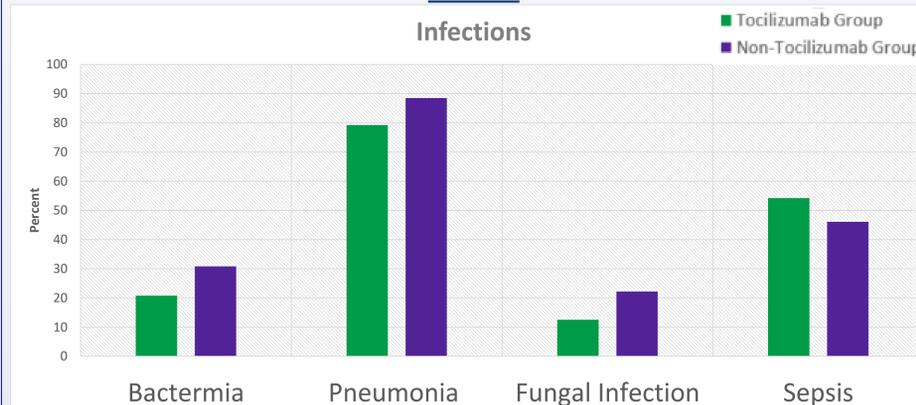
Objectives

- Describe if there is a difference in rates of infections in critically ill ICU patients diagnosed with COVID-19 pneumonia that received tocilizumab to those that did not
- Hypothesis:** is that patients the tocilizumab will have higher rates of infection but lower rates of mechanical ventilation compared to those that did not receive tocilizumab

Methods

- A IRB retrospective approved chart review
- Patients admitted to the Medical Intensive Care Unit at Regions Hospital for treatment of COVID-19 pneumonia
- February 1st, 2021 to December 31st, 2021
- Inclusion
 - Age 18 years or older
 - Confirmed COVID-19 infection by positive PCR laboratory test
 - Admitted to the Medical Intensive Care Unit at Regions Hospital
- Exclusion
 - Patients that are immunosuppressed (HIV/AIDS, recent chemotherapy, transplant, chronic steroid use, use of immunomodulators)
 - Pregnancy
 - Bacterial or fungal infection confirmed by laboratory cultures prior to ICU admission
 - Latent or active tuberculosis
 - Those that elected to not have their medical information used for research purposes

Results



Conclusions

- This study is still ongoing and results are based on preliminary data
- Tocilizumab use appears to be associated with:
 - Lower rates of infection besides sepsis
 - Longer hospital length of stay
 - More ventilator free days
 - Higher mortality
- Additional studies are needed utilizing larger patient populations to determine statistical significance of the differences found in this study

Limitations

- This study is retrospective in nature and difficult to directly compare therapies
- Advanced methods to draw conclusions from observation data beyond scope and power of this study
- The recommended, approved, and available therapies for COVID-19 pneumonia have change drastically since the start of the pandemic
- The clinical course of COVID-19 pneumonia is unpredictable from patient to patient

Future Directions

- Study is still ongoing and collecting more data
- A much larger scale study looking at the clinical course for all Regions Hospital inpatients admitted/treated for COVID-19 is currently underway

References

- RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med.* 2021;384(8):693-704. doi:10.1056/NEJMoa2021436
- Salama C, Han J, Yau L, et al. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. *N Engl J Med.* 2021;384(1):20-30. doi:10.1056/NEJMoa2030340
- Rosas IO, Bräu N, Waters M, et al. Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia. *N Engl J Med.* 2021;384(16):1503-1516. doi:10.1056/NEJMoa2028700
- Product Information: ACTEMRA(R) intravenous, subcutaneous injection, tocilizumab intravenous, subcutaneous injection. Genentech Inc (per FDA), South San Francisco, CA, 2019
- Emergency Use Authorization. U.S. Food and Drug Administration. <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

Acknowledgements

- Mary Ullman Emmerich, PharmD, BCPS, BCIDP - Program Director
- Adis Keric, PharmD, BCPS - Research Advisor
- Wrenda Teeple, PharmD - Study Proposal Reviewer