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562. Tocilizumab for the Treatment of Severe COVID-19: A Retrospective, Multi-Center, Case-Matched Series

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Session: P-21. COVID-19 Treatment

Background: At the time of this writing, there is no FDA approved medication for the treatment of COVID-19. One medication currently under investigation for COVID-19 treatment is tocilizumab, an interleukin-6 (IL-6) inhibitor. It has been shown there are increased levels of cytokines including IL-6 in severe COVID-19 hospitalized patients attributed to cytokine release syndrome (CRS). Therefore, inhibition of IL-6 receptors may lead to a reduction in cytokines and prevent progression of CRS. The purpose of this retrospective study is to utilize a case-matched design to investigate clinical outcomes associated with the use of tocilizumab in severe COVID-19 hospitalized patients.

Methods: This was a retrospective, multi-center, case-matched series matched 1:1 on age, BMI, and days since symptom onset. Inclusion criteria included ≥ 18 years of age, laboratory confirmed positive SARS-CoV-2 result, admitted to a community hospital from March 1st – May 8th, 2020, and received tocilizumab while admitted. The primary outcome was in-hospital mortality. Secondary outcomes included hospital length of stay, total mechanical ventilation days, mechanical ventilation mortality, and incidence of secondary bacterial or fungal infections.

Results: The following results are presented as tocilizumab vs control respectively. The primary outcome of in-hospital mortality for tocilizumab (n=26) vs control (n=26) was 10 (38%) vs 11 (42%) patients, p=0.777. The median hospital length of stay for tocilizumab vs control was 14 vs 11 days, p=0.275. The median days of mechanical ventilation for tocilizumab (n=21) vs control (n=15) was 8 vs 7 days, p=0.139, and the mechanical ventilation mortality was 10 (48%) vs 9 (60%) patients, p=0.463. In the tocilizumab group, for those expired (n=10) vs alive (n=16), 10 (100%) vs 7 (50%) patients respectively had a peak ferritin > 600 ng/mL, and 6 (60%) vs 8 (50%) patients had a peak D-dimer > 2,000 ng/mL. The incidence of secondary bacterial or fungal infections within 7 days of tocilizumab administration occurred in 5 (19%) patients.

Conclusion: These findings suggest that tocilizumab may be a beneficial treatment modality for severe COVID-19 patients. Larger, prospective, placebo-controlled trials are needed to further validate results.

Disclosures: Christian Cheatham, PharmD, BCIDP, Antimicrobial Resistance Solutions (Shareholder)

563. Tocilizumab in the Treatment of Critical COVID-19 Pneumonia

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Session: P-21. COVID-19 Treatment

Background: The anti-interleukin-6 receptor monoclonal antibody tocilizumab has been proposed as a treatment for COVID-19 pneumonia although the efficacy remains unknown.

Methods: Patients with COVID-19 confirmed by nasal swab PCR for SARS-CoV-2 who were admitted to Stony Brook University Hospital in Suffolk County, New York between March 10th and April 2nd and received tocilizumab while undergoing mechanical ventilation in any intensive care unit were retrospectively analyzed from data available in the electronic medical record. Baseline characteristics and clinical outcomes were compared to mechanically ventilated patients admitted during the same time period who received standard hospital protocol.

Results: Forty-five patients received tocilizumab compared to seventy controls. Mean dose of tocilizumab given was 4.8mg/kg and mean time to receipt from initial intubation was 2.5 days. Baseline demographic characteristics, inflammatory markers, treatment with corticosteroids, and SOFA scores were similar between the two cohorts (Table 1). Patients who received tocilizumab had significantly lower Charlson co-morbidity index (2.0 versus 3.0, p = 0.01) and higher temperature (38.7 C versus 38.2 C, p = 0.004) than controls. There was no significant association between receipt of tocilizumab and the rate of extubation within fourteen days (44.4 percent versus 34.2 percent; OR = 1.53, 95% C.I. 0.71 – 3.30), discharge from hospital (51.1 percent versus 40.0 percent; OR = 1.568, 95% C.I. 0.737 – 3.337), or mortality (31.1 percent versus 41.4 percent; OR = 0.639, 95% C.I. 0.290 – 1.4407) (Table 2). Patients who were administered tocilizumab within two days of intubation had increased likelihood of extubation within fourteen days compared to those who were treated later (OR = 3.50, 95% C.I. 1.01 – 12.18). There was no observed increased risk of secondary infection in patients given tocilizumab (28.9 versus 25.7, OR = 1.1736, 95% C.I. = 0.507 – 2.714).

Table 1: Patient Demographics and Baseline Characteristics

	Tocilizumab (n=45)	Controls (n=70)	P-value
Mean age – yr (SD)	56.2 (14.7)	60.6 (13.4)	0.0935
Male – no (%)	29 (64.4)	51 (72.9)	0.3386
Race – no (%) White non-Hispanic	19 (42.2)	33 (47.1)	0.4416
Hispanic	20 (44.4)	27 (38.6)	
Black/AA	3 (6.7)	3 (4.3)	
Asian	3 (6.7)	11 (15.7)	
Mean BMI – kg/m^2 (SD)	30.7 (5.3)	31.3 (6.9)	0.5820
Tmax on ICU admission – degree C, mean (SD)	38.7 (0.82)	38.2 (0.89)	0.0042
C-reactive protein on ICU admission – mg/dL, median (IQR)	19.5 (15.7)	17.6 (18.0)	0.8120
Ferritin baseline – ng/mL, median (IQR)	1507 (1518)	1462[a] (1435)	0.8950
Interleukin-6 baseline – pg/mL, median (IQR)	81.6 (99.4)	92.3[b] (131.5)	0.6569
Corticosteroid treatment – no (%)	33 (73.3)	55 (78.6)	0.5178
Hydroxychloroquine treatment– no (%)	43 (95.6)	65 (92.9)	0.7030
SOFA score, median (IQR)	5.0 (3.0)	5.0 (5.0)	0.3539
Charlson Comorbidity Index, median (IQR)	2.0 (3.0)	3.0 (3.0)	0.0141

a) n = 68; b) n = 56

Table 2: Primary Outcomes

	Tocilizumab (n=45)	Controls (n=70)	OR (95% C.I.)	P-value
Extubation in 14 days – no (%)	20 (44.4)	24 (34.2)	1.533 (0.712-3.304)	0.2751
Discharged – no (%)	23 (51.1)	28 (40.0)	1.568 (0.737-3.337)	0.2429
Death – no (%)	14 (31.1)	29 (41.4)	0.639 (0.290-1.4407)	0.2658
Secondary infection – no (%)	13 (28.9)	18 (25.7)	1.1736 (0.507-2.714)	0.7081

Conclusion: Tocilizumab was not associated with a significant improvement in rate of extubation, hospital discharge, or reduction in mortality in this retrospective cohort study of mechanically ventilated patients with COVID-19 pneumonia. Further studies are needed to determine whether earlier treatment may result in improved outcomes.

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564. Tocilizumab Induces Rapid, Sustained Improvement of Inflammatory Markers in COVID-19.

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Session: P-21. COVID-19 Treatment

Background: Frequent observation of increasing fever and rising inflammatory markers late after onset of COVID-19 suggests Cytokine Release Syndrome (CRS, "Cytokine Storm") may contribute to pathophysiology. Tocilizumab (TCZ), a monoclonal antibody targeting the receptor for the pro-inflammatory cytokine, IL-6, is effective in suppressing pathological inflammation in several rheumatological diseases. After administering TCZ to COVID-19 patients with suspected CRS, we observed a sharp fall in inflammatory indices. We analyzed this effect using results from the first 19 COVID-19 patients receiving TCZ at our hospital.

Methods: Data for all patients with confirmed COVID-19 who received TCZ at our center, a 200 bed community hospital in New England, were extracted from the Electronic Medical Record, including demographics, body temperature, C-Reactive Protein (CRP), IL-6 levels, clinical severity on the Ordinal Scale for Clinical Improvement (OSCI), and clinical outcome (recovery/discharge home, partial recovery/discharge rehab, death). Results were tabulated and statistical significance of changes in indices pre- and post- TCZ assessed by Wilcoxon Signed-Rank Test.

Results: 19 patients received TCZ: 16 got 400mg x1, 2 got 400 mg x2, 1 got 660 mg x1. Median age was 64 years (range: 44–94), 68% male. Mean interval from symptom onset to receiving TCZ was 11.5 days. Mean IL-6 was 145 pg/mL. Demographics, OSCI