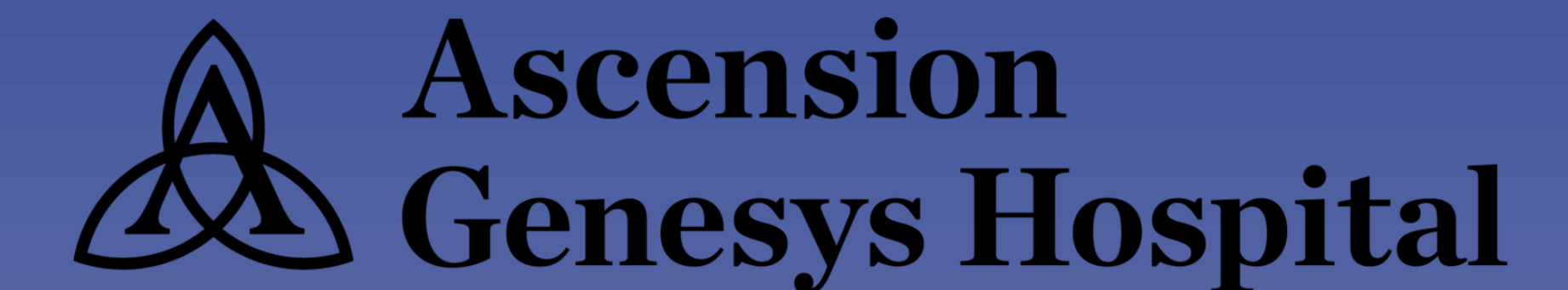# Treatment for Progressive Respiratory Distress During the COVID-19 Pandemic: A Case Series

Virginia LaBond, MD; Kristen Hartnett, DO; Jennifer R. Hella, MPH; Roya Z. Caloia, DO; Kimberly R. Barber, PhD

Ascension Genesys Hospital
Medical Education
Grand Blanc, MI

Introduction

- The World Health Organization (WHO) declared COVID-19 a pandemic on March 11th, 2020.[1]

- Clinical features of patients diagnosed with COVID-19 in early 2020 suggested that up to 29% of severe cases had a progression of respiratory injury developing into acute respiratory distress syndrome (ARDS).[2]

- ARDS was largely attributed to a severe cytokine storm that many patients were experiencing.[3]

- Pathologic characteristics of patients dying of COVID-19 demonstrated interstitial pulmonary infiltrates, pulmonary edema and increased serum concentrations of highly pro-inflammatory cytokines including interleukin-6.[4]

- Tocilizumab, was an early front runner in the treatment for severely ill Covid-19 patients, a monoclonal antibody that inhibits interleukin-6.[5]

- Randomized trials from the first half of 2020 suggested slight but significantly less clinical deterioration among patients treated with tocilizumab but no mortality benefit.[6]

Hypothesis

Response to Toculizumab will demonstrate improving respiratory status and tampering of the inflammatory activation.

Methods

- Case series was performed at a 380-bed Midwestern suburban community hospital.

- IRB approval was given on June 9, 2020 by the Ascension Genesys Hospital IRB.

- Pharmacy records were used to identify all patients receiving Tocilizumab (TCB) for the treatment of COVID-19 from 03/01/2020 - 05/31/2020.

- Retrospective chart review was performed for day 0 through day 30 of hospitalization for the 15 identified patients.

- Demographics, respiratory status pre and post Tocilizumab administration, adjunct medications administered, laboratory values, imaging and final outcomes were abstracted.

- Descriptive analysis using means and standard deviations to report on continuous variables such age, dosage, and time was completed.

- Rates and percentages were calculated for dichotomous and frequency variables such as gender, comorbid conditions, respiratory status and medication.

Results

Table 1: Demographics (N=15)

Age (mean, SD)	60.1 (15.6)
Gender (n,%)	
Male	9 (60)
Female	6 (40)
Race (n,%)	
Caucasian	7 (46.7)
African American	6 (40)
Asian	1 (6.7)
Missing	1 (6.7)
Comorbidities (n,%)	
Diabetes	10 (66.7)
COPD	2 (13.3)
Obesity	6 (40)
Hypertension	11 (73.3)
Hyperlipidemia	7 (46.7)

Table 2: Adjunct COVID-19 Pharmacotherapy

Treatment	N (%)
Tocilizumab	15 (100)
Azithromycin	14 (93.3)
Plaquenil	12 (80)
Methylprednisone	15 (100)
Remdesivir	1 (6.7)
Convalescent Plasma	1 (6.7)

Table 3: Frequency of Inflammatory Marker Evaluation

CRP	N (%)
Day -1	2 (13.3)
Day 0	4 (26.6)
Day +1	3 (20.0)
Ferritin	
Day -1	5 (33.3)
Day 0	8 (53.3)
Day +1	8 (53.3)
D-Dimer	
Day -1	5 (33.3)
Day 0	9 (60.0)
Day +1	10 (66.7)

Figure 1: Respiratory status following Tocilizumab administration (respiratory status over time)
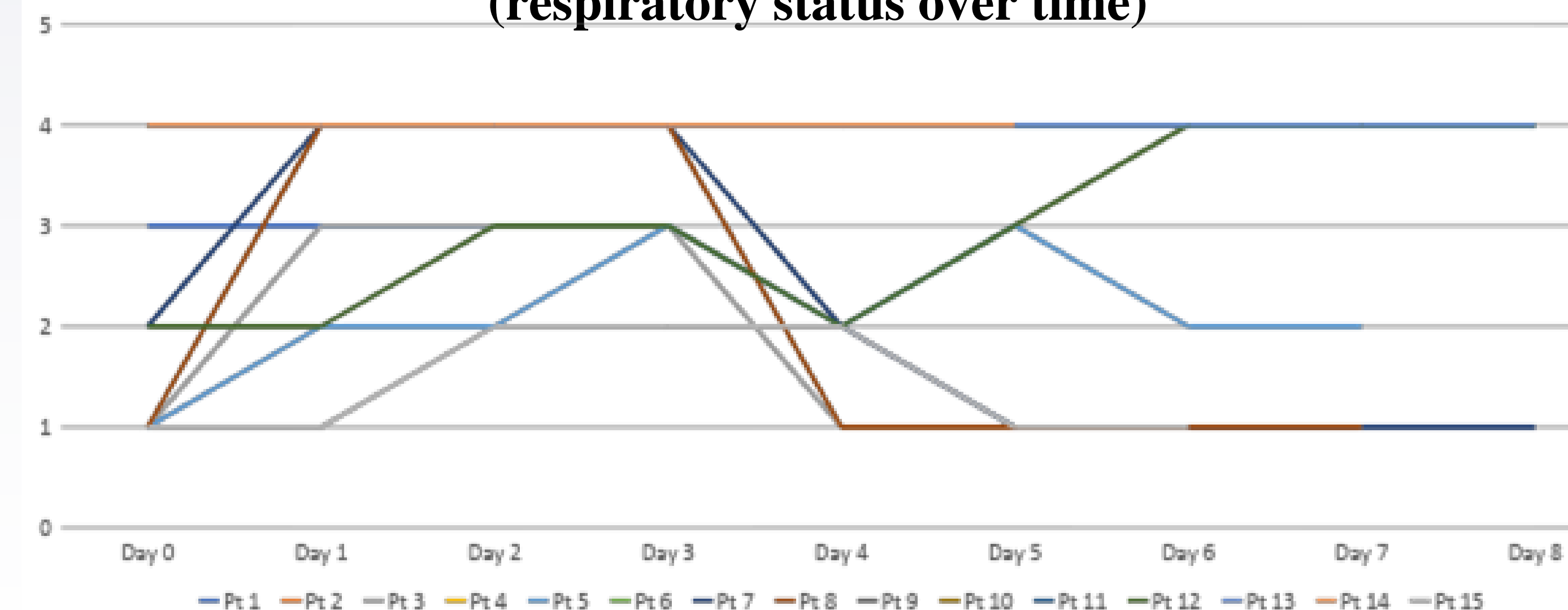
Discussion

- Over the three month period in which we reviewed patients treated with tocilizumab for COVID-19, there was significant variation in patients evaluation and treatment regimen.

- Tocilizumab was proposed to be effective by decreasing cytokine storm and inflammatory esponse,[5,7] yet when reviewing the frequency of evaluation of inflammatory markers (D-dimer, CRP, Ferritin) a startlingly low number of patients had these markers checked on the day of tocilizumab administration and few were re-evaluated in the day after administration of tocilizumab to follow progression of illness severity via inflammatory markers.

- The lack of re-evaluation could indicate a lack of confidence in the treatment, lack of confidence in the evidence, or even an intensifying reliance on clinical judgement during the height of the pandemic.

- One of the more reliable indications of patients' illness severity and progression was their respiratory status, Figure 1 does not demonstrate the improvement of respiratory status one would expect following the drug's administration.

- Lack of strong, peer-reviewed evidence based medicine led to an extemporaneous reaction and a sprint for superior treatment options.

- Demonstrates pitfalls and challenges of medical treatment and protocol formation during the pandemic spread of a newly emerging pathogen.

- We must define indications for Tocilizumab initiation and monitoring: which clinical indications should determine use, dosage and frequency of medication administration and frequency with which inflammatory markers should be monitored post-administration.

Conclusion

Emerging pathogen with no protocol places physicians in a quagmire of expeditious decision making, with ever evolving information and transformation of protocols that facilitates chaos.

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