

Tocilizumab Use in COVID-19: Act(emra) to INHIBIT Intubation and Decompensation Debra Willner, PharmD¹, Ilanit Zada, PharmD¹, Jose Ricardo Trigueros², MD, Nigam Patel, MD³, Judith Berger, MD⁴, Victoria Bengualid, MD⁵

BACKGROUND

- COVID-19 affects many organs leading to various complications
- Many complications are thought to arise from a cytokine storm, and inflammatory reaction caused by a release of pro-inflammatory cytokines, mainly IL-6, IL-10, tumor-necrosis factors, and growthcolony-stimulating factors, [1]
- Tocilizumab (Actemra[®]) is an IL-6 receptor inhibitor that binds to 6 receptors and blocks this specific inflammatory pathway
- There have been several case series' and retrospective reviews of tocilizumab use for the prevention of the cytokine storm inflammatory reaction in COVID-19
- The first report was a case series of 21 patients treated with a one time dose of tocilizumab in Wuhan, China; most of the patients experienced significant improvements in their symptoms, laborated markers, after tocilizumab[2]
- We wanted to evaluate the outcomes of our patients treated with tocilizumab, and the relationships between the inflammatory markers and clinical outcomes
- This was a retrospective chart review evaluating patients treated with tocilizumab 400mg for COVID-19 from March 30th-May 16th, 2020
- Our objectives were to evaluate outcomes of patients treated with tocilizumab in relation to both respiratory status and inflammator markers at treatment initiation

RESULTS

84 patients were treated with tocilizumab: 38 of these patients were started on tocilizumab when intubated. Outcome in these 2 groups of patients were significantly different:



*Treatment success defined as hospital discharge **Treatment failure defined as any escalation of care: intubation, death, or continued hospitalization

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					RESULTS			
	Baseline Characteristics (n=84)				Outcomes by Markers			
		Not Intubated (N=46)	Intubated (N=38)	P-value	Δαο	Total Number	Treatment Failure	P-value
A٤	ge (median)	59	55	0.26	<65	55 29	52% 62%	0.06
Ge	ender Male Female	70% 30%	68% 32%	0.91	Gender Male Female	58 26	55% 58%	0.54
Et	hnicity Hispanic Non-Hispanic	65% 35%	45% 55%	0.06	Ethnicity Hispanic Non-Hispanic	47 37	57% 54%	0.55
Ra	ace Black Caucasian	65% 35%	61% 39%	0.5	Past medical histor Diabetes No diabetes	y 29 55	66% 51%	0.003
Pa	ast Medical History Hypertension Diabetes	41% 35%	44.7% 34%	0.44 0.06	BMI (kg/m²) <30 ≥30	38 46	47% 63%	0.001
De	Asthma/COPD BMI (kg/m ²)	19% 28.9	13% 30.5	0.79 0.45	II-6 (pg/mL) <1000	70	50%	0.0001
Da (m	T-max (°F) IL-6 (pg/mL) C-Reactive Protein ng/dL)	100.5 116.5 21.9	101.4 233.5 24.9	0.08 0.08 0.07	≥1000 CRP (mg/dL) <20 ≥20	8 25 55	88% 48% 56%	0.1



Figure 1 Concomitant Medications in Treatment Success Group

MORTALITY	Tocilizumab	Sample Size	Hospital Wide	Sample Size	P-value
Intubated/ICU	63%	38	87%	175	<0.0001
Non-Intubated	26%	46	16%	579	0.006
Overall Mortality	43%	84	33%	754	0.03



Aortality in non-intubated IL-6 inhibitor patients and overall nortality in IL-6 inhibitor patients were significantly higher than ospital-wide patients; however, the sample sizes vary significantly Comorbities: patients with BMI's of 30 or above and patients with diabetes had a higher rate of treatment failure (p < 0.05) • Laboratory markers: patients with IL-6 levels of 1000 or above had higher rates of treatment failure (p = 0.0001); however, given the small sample size larger studies are required for further analysis

1. Zhong, J., Tang, J., Ye, C. and Dong, L., 2020. The immunology of COVID-19: is immune modulation an option for treatment?. *The Lancet* Rheumatology 2. Xu, X., Han, M., Li, T., Sun, W., Wang, D., Fu, B., Zhou, Y., Zheng, X., Yang, Y., Li, X., Zhang, X., Pan, A. and Wei, H., 2020. Effective treatment of severe COVID-19 patients with tocilizumab. Proceedings of the National Academy of Sciences, 117(20), pp.10970-10975. 3. Toniati, P., Piva, S., Cattalini, M., et al, 2020. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. Autoimmunity Reviews, p.102568.

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DISCUSSION

overall mortality in patients who received an IL-6 inhibitor was 43%. Aortality in patients who received IL-6 inhibitor when intubated 63%) compared to patients who were not intubated(26%) was ignificantly higher (p = 0.005)

As there is no control group we compared these results to the overall mortality of hospitalized COVID-19 patients. The mortality in ntubated IL-6 inhibitor recipients were lower than hospital wide nortality in intubated patients (p < 0.05)

CONCLUSIONS

Based on the retrospective results of this study and comparison to a historic "control" group, the use of tocilizumab was associated with decreased mortality in intubated patients

Most patients analyzed did not receive concomitant investigational therapies necessitating the need for further trials assessing the benefit of multiple treatment options

Randomized control trials are needed to determine the true benefit of tocilizumab in COVID-19

REFERENCES