Critically Ill patients Receiving Tocilizumab Compared With Those Not Receiving Tocilizumab for Treatment of COVID-19

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Background

At the onset of the COVID-19 pandemic, the need for potential therapies for increasing numbers of critically ill patients was evident.

- COVID mortality driven by respiratory failure and ARDS [1].
- Increased release of pro-inflammatory cytokine IL-6 in severe acute respiratory syndrome coronavirus 1 (SARS), Middle East respiratory syndrome (MERS) and COVID-19 [2,3].
- Increased IL-6 mediates development of pulmonary damage and ARDS [2].
- Tocilizumab, an IL-6 receptor blocker, is FDA-approved for chimeric antigen receptor (CAR) T cell-induced severe or life threatening cytokine release syndrome (CRS) [4].

Objective

To describe patient characteristics and clinical outcomes associated with tocilizumab compared with those not receiving tocilizumab in critically ill patients with COVID-19.

Methods

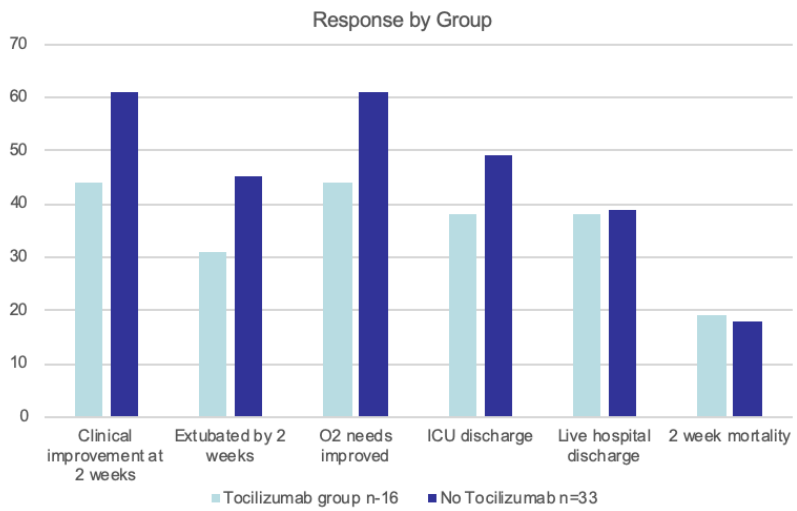
- Retrospective cohort study evaluating critically ill patients with COVID-19 treated within a large health system, Atrium Health.
- All adult patients admitted to an intensive care unit (ICU) with SARS-CoV-2 between March 10 and April 5, 2020 were included.
- Followed for 2 weeks from ICU admission or until discharge or death.
- Baseline characteristics and clinical outcomes of patients receiving tocilizumab versus those not receiving tocilizumab were compared.
- Primary endpoint: clinical improvement 2 weeks after ICU admission (decreased supplementary oxygen requirements, transfer out of the ICU, and live discharge from the hospital).
- Secondary endpoints: overall mortality, proportion of patients extubated, and time to extubation (if received mechanical ventilation) within two weeks of ICU admission.

Results

Table 1. Baseline characteristics

Characteristics	Tocilizumab N = 16	No tocilizumab N = 33	P-value
Age (years, median, IQR)	62 (45, 72)	66 (56, 71)	0.28
Male sex (n, %)	13 (81)	26 (79)	>0.99
Race (n, %) African American Caucasian Other	11 (69) 4 (25) 1 (6)	26 (79) 7 (21) 0	0.33
Weight (kg, median, IQR)	92 (87, 111)	91 (80, 113)	0.73
Comorbidities (n, %) Overweight/obese (BMI >25) Cardiovascular disease Pulmonary disease Diabetes mellitus Renal disease Liver disease Immunocompromise [1]	15 (94) 7 (44) 4 (25) 5 (31) 3 (19) 1 (6) 1 (6)	27 (82) 23 (70) 9 (27) 18 (55) 5 (15) 0 2 (6)	0.40 0.08 >0.99 0.13 >0.99 0.33 >0.99
Time from symptom onset to positive test (days, median, IQR)	4 (3, 6)	4 (2, 6)	0.65
Time from symptom onset to intubation (days, median, IQR)	N = 13 7 (6, 10)	N = 20 7 (6, 10)	0.90
Maximum temperature within 24 hours of ICU admission (median, IQR,°F)*	101.2 (100.2, 103.0)	101.4 (99.7, 102.7)	0.46
Baseline IL-6 (pg/mL, median, IQR)	N = 9 249 (130, 554)	N = 9 128 (87, 155)	0.06
Maximum CRP within 24 hours of ICU admission (median, IQR)	N = 14 20 (17, 28)	N = 31 17 (9, 23)	0.07
Oxygen support at baseline (n, %) Mechanical ventilation NIPPV High-flow nasal cannula Low-flow nasal cannula Ambient air ECMO	10 (63) 0 1 (6) 5 (31) 0 0	16 (49) 2 (6) 7 (21) 8 (24) 0 0	0.43
Presence of ARDS (n, %)	14 (88)	20 (60.6)	0.10
Berlin criteria score for ARDS (n, %)	11 (68.8)	19 (57.6)	0.45
APACHE II score (median, IQR)	15 (10, 19)	14 (9, 20)	0.80
Receipt of corticosteroids	1 (6)	7 (21)	0.18
Any concomitant COVID-directed therapy Hydroxychloroquine Other [2]	14 (88) 14 (88) 0	27 (82) 27 (82) 3 (9)	>0.99 >0.99 0.54
Receipt of empiric antimicrobials (n, %)	10 (63)	25 (76)	0.50

Table 2. Clinical outcomes



- Forty-nine patients were identified with SARS-CoV-2 who were admitted to an ICU, with 16 patients receiving tocilizumab.
- 63% of patients who received tocilizumab were intubated within 24 hours of ICU admission, versus 49% of patients not receiving tocilizumab
- The median time from symptom onset to tocilizumab administration was 11 days and median time from ICU admission to tocilizumab administration was 3 days.
- Mortality was similar between the two groups, 19% of tocilizumab patients and 18% of non-tocilizumab patients.

Additional results

- In our study, tocilizumab was administered at a median of 11 days from symptom onset, with 88% already showing signs of ARDS and 81% being mechanically ventilated

Discussion

- Clinical outcomes at 2 weeks following ICU admission were similar between patients regardless of tocilizumab treatment
- Fevers and inflammatory markers improved in patients receiving tocilizumab, but there were no associated improvements in clinical outcomes (oxygen support, ICU or hospital discharge, or mortality).
- There was no observed increased risk of adverse outcomes in patients receiving tocilizumab.
- Tocilizumab's lack of efficacy in our population may have been due to late use in the disease
- This difference in disease severity may explain the differences in improvement when compared previous studies evaluating tocilizumab efficacy.
- Limitations of this study are the non-randomized treatment and control groups, as it is retrospective in design. This study was also underpowered to reveal differences from tocilizumab treatment, and patients included received other therapies for COVID-19, so it is unclear if this impacted clinical outcomes.

Conclusions

- Clinical outcomes were similar regardless of Tocilizumab treatment.
- Tocilizumab did demonstrate decreases in serum CRP as well as reduction of fevers.
- Future studies examining earlier use of tocilizumab in the disease course are needed, as well as identifying clinical characteristics to assist with selection of the appropriate patient population who will benefit from this intervention.

References

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Disclosures

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or this presentation.