Real-world Experience Highlighting Tocilizumab Use in the Treatment of COVID-19 Christina Maguire, PharmD, BCIDP¹ • Adrienne Terico, PharmD, BCPS, BCIDP² • Hinal Patel, PharmD, BCPS³ • George L. Anesi, MD, MSCE⁴ • Kathleen O. Degnan, MD⁵ Lauren Dutcher, MD, MSCE⁵ • Keith W. Hamilton, MD⁵ • Nuala J. Meyer, MD, MS⁴ • Naasha Talati, MD, MSCR⁵ • Stephen Saw, PharmD, BCIDP⁶

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Background

- The Food and Drug Administration issued an emergency use authorization for tocilizumab (TCZ) for treatment of COVID-19 in patients requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation in early 2021.¹
- In January 2021, the University of Pennsylvania Health System (UPHS) COVID-19 Therapeutics Committee added TCZ to the treatment algorithm for COVID-19 given a favorable mortality benefit demonstrated in the REMAP-CAP trial.²
- Despite seeing positive results in other trials, there still remain unanswered questions surrounding the use of TCZ.³

Objectives

- The primary objective of this study is to characterize the efficacy and safety of TCZ for treatment of COVID-19 in a real world setting.
- Secondary objectives include providing detailed data regarding disposition status, adverse events, and steroid usage in TCZ patients.

Methods

- **Study Design:** retrospective, multicenter cohort study
- **Study Period**: January 29th, 2021 to June 30th, 2021
- **Population**: Any patient who received TCZ (8 mg/kg; max dose 800 mg once) for treatment of confirmed COVID-19 within five of the UPHS centers per UPHS COVID-19 Therapeutics guidance.

| | Figure 1: UPHS COVID-19 Therapeutics Guid | da | nce for TCZ Use |
|---|---|----|---------------------------------|
| | Inclusion Criteria | Ε | xclusion Criteria |
| • | <14 days of acute symptoms and <72 hours of hospitalization | • | Platelets ≤50 ALT and AST ≥3 |
| • | Requiring high-flow nasal cannula with FiO2 ≥40%, non-invasive positive pressure ventilation, or mechanical ventilation | | times upper limit of normal |
| • | In intensive care unit (ICU), ICU eligible, and/or clinically deteriorating or high-risk of deterioration even if not in the ICU (as long as patient fits other inclusion criteria) | | |
| • | <24 hours of ICU/ICU eligible for severe respiratory failure due to COVID-19 | | |

| Table 1. Dasenne characteristics | N=134 | Table 5: Clinical Outcomes and I | Disposition |
|---|--------------------|---|------------------|
| ale, n (%) | 74 (55.2) | Mortality within 30 days of TCZ, n/N (%) | 28/134 (20.9) |
| ge (years), mean (SD) | 58.3 (15.5) | WHO ordinal scale 5 at baseline, n/N (%) | 23/117 (19.7 |
| ody mass index (kg/m²), mean (SD) | 33.9 (9.5) | WHO ordinal scale 6 & 7 at baseline, n/N (%) | 5/17 (29.4) |
| Z | | Immunocompromised, n/N (%) | 8/19 (42.1) |
| Time from admission to order entry (hours), median | 22 (13.2 to 41.5) | Days from TCZ to mortality, median (IQR) | 12.5 (5 to 18.3) |
| (IQR) | | Days from admission to mortality, median (IQR) | 15 (6.8 to 20) |
| Time from hospital admission to ICU admission | 7/(/ 3 + 0.233) | Discharged by day 30, n/N (%) | 96/106 (90.6) |
| (hours), median (IQR) | 7.4 (4.5 to 25.5) | Home | 68/96 (70.8) |
| ICU at time of order entry, n (%) | 102 (76.1) | Skilled nursing facility or rehabilitation | 20/96 (20.8) |
| HO ordinal scale at time of TCZ order entry, n (%) | | Long term acute care bosnital | 8/96 (8 3) |
| 5 | 117 (87.3) | Mortality within 60 days of TC7 n/N/(%) | 2/12/(25/) |
| 6 | 7 (5.2) | MULO endinel cecle E et beceline in (NL (%) | 29/117 (22.4) |
| 7 | 10 (7.5) | WHO ordinal scale 5 at baseline, n/N (%) | |
| te of symptom onset documented, n (%) | 100 (74.6) | WHO ordinal scale 6 & 7 at baseline, n/N (%) | 6/1/(35.3) |
| Time from symptom onset to administration (days), | 7.3 (2.7) | | |
| mean (SD) | | Figuro 7. Advorco Evor | atc |
| ccination status at time of TCZ order entry, n (%) | | rigule 2: Auvelse Evel | 115 |
| Fully vaccinated | 3 (2.2) | | |
| Partially vaccinated | 12 (9) | Advers | se Events |
| Unvaccinated | 104 (77.6) | | |
| Unknown | 15 (11.2) | Adverse drug events occur | red in 45 |
| morbid conditions, n (%) | | out of 134 (33.6%) of patie | nts. |
| Diabetes mellitus | 46 (34.3) | Honatitic occurred in 6.7% | of nationts |
| Immunocompromised | 19 (14.2) | nepatitis occurred in 0.776 | or patients. |
| Chronic kidney disease | 18 (13.4) | | |
| Heart failure | 18 (13.4) | Bacterial Infections Fungal | Infections |
| Asthma | 13 (9.7) | (40/134, 30%)* (4/13 | 34, 3%) |
| Chronic obstructive pulmonary disease | 10 (7.5) | ff o o o | |
| Cystic fibrosis | 1 (1) | $ \neg \exists \land \land$ | |
| Liver cirrhosis | 1 (1) | | |
| | | | |
| | | 65% 25% 12.5% 25% | 75% |
| | • | | |
| Table 2: Concomitant Medication | ions | *Other: intra-abdominal (5%), Other (17.5%) | |
| edications received within 30 days of TCZ, n (%) | | | |
| Corticosteroids | 134 (100) | Figure 7 . | |
| Remdesivir | 131 (97.8) | rigure 3: | |
| Monoclonal antibody | 3 (2.2) | | • |
| Convalescent plasma | 2 (1.5) | Corticosteroid Use with Tocilizi | umab |
| Inhaled nitric oxide or prostacyclin | 5 (3.7) | 100 100 | |
| rticosteroids, continued | | 80 | |
| Total prednisone equivalents (mg), median (IQR) | 400 (335.6 to 480) | b b b c c c c c c c c c c | |
| Total corticosteroid length of therapy (days), median | 10 (9 to 12) | 40 | |
| (IQR) | | Jo 20 | |
| Average daily prednisone equivalent (mg), median | AO(AO + O(A2) = 7) | 0 13.4 19.4 | 9 |
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| Kesults | | | |
|---|---|--|--|
| Table 1: Baseline Characteristics | N=134 | Table 3: Clinical Outcomes and | Disposition |
| Male, n (%) | 74 (55.2) | Mortality within 30 days of TCZ, n/N (%) | 28/134 (20.9) |
| Age (years), mean (SD) | 58.3 (15.5) | WHO ordinal scale 5 at baseline, n/N (%) | 23/117 (19.7) |
| Body mass index (kg/m ²), mean (SD) | 33.9 (9.5) | WHO ordinal scale 6 & 7 at baseline, n/N (%) | 5/17 (29.4) |
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| 6 | 7 (5.2) | MULO endinel cecle E et beceline in (NL (%) | 34/134(23.4) |
| 7 | 10 (7.5) | WILL ordinal scale 5 at baseline, n/N (%) | 28/11/(23.9) |
| Date of symptom onset documented, n (%) | 100 (74.6) | WHO ordinal scale 6 & 7 at baseline, n/N (%) | 6/1/ (35.3) |
| Time from symptom onset to administration (days), | 7.3 (2.7) | | |
| mean (SD) | | Figura 7. Advance Free | ata |
| /accination status at time of TCZ order entry, n (%) | | rigure 2: Auverse Evel | 113 |
| Fully vaccinated | 3 (2.2) | | |
| Partially vaccinated | 12 (9) | Advers | se Events |
| Unvaccinated | 104 (77.6) | | |
| Unknown | 15 (11.2) | Adverse drug events occur | red in 45 |
| Comorbid conditions, n (%) | | out of 134 (33.6%) of patie | nts. |
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Discussion

- Use of TCZ in severe COVID-19 resulted in an observed 30 day mortality rate of 20.9%. An additional 6 patients expired at day 60 from TCZ administration (34/134, 25.4%).
- A small percentage of our cohort was immunocompromised (14.2%). These patients experienced higher mortality compared to the rest of our cohort (42.1%).
- For those alive at day 30, only 9.4% remained hospitalized at day 30. A majority of patients were discharged home (70.8%).
- All patients received corticosteroids. The median prednisone equivalents and days of therapy align with dexamethasone dosing and duration recommendations for severe COVID-19.
- Approximately one third of patients developed a bacterial infection while fungal infections represented less than 5% of patients.
- Our study has multiple limitations including lack of generalizability given hybrid inclusion and exclusion criteria when compared to landmark trials and retrospective design.

Conclusion

- A majority of deaths in patients receiving TCZ for severe COVID-19 occurred by day 30. Mortality at days 30 and 60 was higher among those with a higher ordinal scale at the time of TCZ dosing (29.4% and 35.3%, respectively).
- In a real world setting, adverse events were observed in approximately one-third of patients treated with TCZ for severe COVID-19.
- Our cohort had a small percentage of immunocompromised patients that experienced a higher mortality rate in comparison to the rest of the cohort. More data is needed regarding use of TCZ in an immunocompromised patient population.

References

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