Received: 24 June 2020 | Revised: 28 August 2020 | Accepted: 8 September 2020

DOI: 10.1111/ajt.16314

BRIEF COMMUNICATION

AJT

Tocilizumab for severe COVID-19 in solid organ transplant recipients: a matched cohort study

Marcus R. Pereira[1] | Meghan M. Aversa[2] | Maryjane A. Farr[3] | Benjamin A. Miko[1] | Justin G. Aaron[1] | Sumit Mohan[4,5,6] | David J. Cohen[4] | Syed A. Husain[4] | Lloyd E. Ratner[4] | Selim Arcasoy[2] | Nir Uriel[3] | Elizabeth X. Zheng[7] | Alyson N. Fox[7] | Demetra S. Tsapepas[8] | Jean C. Emond[8] | Elizabeth C. Verna[7]

[1]Department of Medicine, Division of Infectious Disease, Columbia University College of Physicians & Surgeons, New York, NY

[2]Lung Transplant Program, Division of Division of Pulmonary, Allergy and Critical Care Medicine, Columbia University College of Physicians & Surgeons, New York, NY

[3]Department of Medicine, Division of Cardiology, Columbia University College of Physicians & Surgeons, New York, NY

[4]Department of Medicine, Division of Nephrology, Columbia University College of Physicians & Surgeons, New York, NY

[5]The Columbia University Renal Epidemiology (CURE) Group, New York, NY

[6]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY

[7]Department of Medicine, Division of Digestive & Liver Diseases, Columbia University College of Physicians & Surgeons, New York, NY

[8]Department of Surgery, Columbia University College of Physicians & Surgeons, New York, NY

Correspondence
Marcus R. Pereira
Email: mp2323@cumc.columbia.edu

The safety and efficacy of tocilizumab for the treatment of severe respiratory symptoms due to COVID-19 remain uncertain, in particular among solid organ transplant (SOT) recipients. Thus, we evaluated the clinical characteristics and outcomes of 29 hospitalized SOT recipients who received tocilizumab for severe COVID-19, compared to a matched control group who did not. Among a total of 117 total SOT recipients hospitalized with COVID-19, 29 (24.8%) received tocilizumab. The 90-day mortality was significantly higher among patients who received tocilizumab (41%) compared to those who did not (20%, $P = .03$). When compared to control patients matched by age, hypertension, chronic kidney disease, and administration of high dose corticosteroids, there was no significant difference in mortality (41% vs 28%, $P = .27$), hospital discharge (52% vs 72%, $P = .26$), or secondary infections (34% vs 24%, $P = .55$). Among patients who received tocilizumab, there was also no difference in mortality based on the level of oxygen support (intubated vs not intubated) at the time of tocilizumab initiation. In this matched cohort study, tocilizumab appeared to be safe but was not associated with decreased 90-day mortality. Larger randomized studies are needed to identify whether there are subsets of SOT recipients who may benefit from tocilizumab for treatment of COVID-19.

KEYWORDS
clinical research/practice, complication: infectious, immune regulation, immunosuppression/immune modulation, infectious disease

Abbreviations: BIPAP, bilevel positive airway pressure; CKD, chronic kidney disease; CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; DM, diabetes mellitus; EBV, Epstein Barr Virus; ESBL, extended-spectrum beta-lactamase; HHV-6, human herpesvirus-6; HTN, hypertension; ICU, Intensive care unit; MRSA, methicillin-resistant Staphylococcus aureus; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on solid organ transplant (SOT) recipients. Although early case series indicated SOT recipients may be at increased risk of severe disease and mortality, subsequent studies have suggested that outcomes may be similar to the general population.[1–7] While data on the antiviral remdesivir have shown a clinical benefit in patients with COVID-19, the optimal management of patients who progress to severe disease after several days of mild symptoms remains less clear.[8,9] The hypothesis that this delayed progression may be attributable to a deleterious hyperinflammatory process or cytokine storm led to a significant interest in immunomodulatory agents such as corticosteroids and tocilizumab, a humanized monoclonal antibody to the IL-6 receptor.[10,11] A large randomized controlled trial has shown that dexamethasone reduces mortality among patients with severe COVID-19.[12] Data on tocilizumab, however, has been less conclusive. Early case series from Wuhan, China, showed promising results while a large retrospective cohort study in Italy demonstrated that administration of tocilizumab in patients with severe COVID-19 reduced the risk of invasive mechanical ventilation or death when compared to patients who did not.[13–15] Unfortunately, phase 3 trials for both tocilizumab and sarilumab, a similar IL-6 receptor inhibitor, were terminated early after not meeting primary and key secondary endpoints.[16,17] However, it remains unknown whether there is a subset of patients who may benefit from this class of agents in particular.

Among SOT recipients, tocilizumab has been used for the treatment of allograft rejection with emerging data on efficacy and safety.[18,19] During the initial months of the pandemic, limited cases of SOT recipients receiving tocilizumab for the treatment of COVID-19 were reported, showing some success with this approach.[20–23] More recently, a multicenter Spanish cohort of 80 kidney transplant recipients who received tocilizumab for severe COVID-19 showed high mortality (32.5%), and more severe disease than patients who did not receive tocilizumab[24]. Interpretation of these results has been limited by the lack of a matched control group, however, and data on tocilizumab use in other SOT recipients are lacking. Here we report on a matched cohort study with off-label tocilizumab in 29 SOT recipients hospitalized with COVID-19.

2 | METHODS

2.1 | Patients

All adult (age >18 years) SOT recipients from Columbia University Irving Medical Center hospitalized with COVID-19 between 3/13/2020 and 4/21/2020 were analyzed. Diagnosis of COVID-19 was confirmed with a positive nasopharyngeal swab for SARS-CoV-2. All patients had a minimum of 90 days of potential observation and were followed until death or discharge. Several patients were included in a previously reported larger cohort of SOT patients[1], but without the tocilizumab-specific analyses described here. This work was approved by the Columbia University institutional review board.

2.2 | Therapeutic approach

All patients with COVID-19 were preferentially considered for investigational agents, including remdesivir, in either clinical trials or expanded access programs. When this was not available, off-label hydroxychloroquine was considered in the early study period.

Intravenous tocilizumab at about 4-8 mg/kg (maximum 800 mg) was considered for patients with at least 7 days of symptoms, progressive respiratory distress, and rising levels of inflammatory markers, including C-reactive protein, ferritin, or IL-6. Some patients received additional doses of tocilizumab when the primary team deemed the initial response to be insufficient. Intravenous methylprednisolone at 1 mg/kg/day was also given in selected patients. In general, baseline immunosuppression was moderately decreased with a particular emphasis on decreasing or discontinuing antimetabolite drugs such as mycophenolate.

2.3 | Analytic approach

All SOT recipients hospitalized with COVID-19 who received tocilizumab were included as cases. For each case, one control matched for age (above or below 60 years), hypertension, chronic kidney disease (CKD), and receipt of high dose corticosteroids for COVID-19 during the hospitalization was selected. The first three matching variables were selected because of their significant correlation with COVID-19 disease severity as described in the literature, including our original cohort.[1] High dose corticosteroids were selected due to the potential confounding of this frequently coadministered additional immunomodulatory therapy, which has more recently been shown to impact treatment outcomes.[12]

Clinical characteristics and outcomes including death and hospital discharge were compared between these groups. Additional complications were also assessed, including secondary infections, venous thrombosis, acute neurological events, and new renal replacement therapy. Non-SARS-CoV-2 viral infections were diagnosed via whole blood or plasma PCR only. Only culture positive bacterial infections were included. In this study, pneumonia, including those that were ventilator associated, was defined as a positive respiratory culture and clinical suspicion for a bacterial pneumonia by the primary team. All positive blood cultures, except those with coagulase-negative staphylococci, were considered to be true infections. Urinary tract infections were not assessed. The clinical characteristics and outcomes of the entire underlying cohort of SOT recipients hospitalized for COVID-19 in this period are also presented in Table S1.

Finally, outcomes among patients who received tocilizumab were also compared between patients who received their initial dose while mechanically ventilated and those who were not ventilated. In this group, median (IQR) levels of inflammatory markers including IL-6,

TABLE 1 Clinical characteristics and outcomes of SOT recipients with COVID-19 who received tocilizumab versus matched controls[a]

	All (n = 58)	Tocilizumab group (n = 29)	Matched control group (n = 29)	*P*-value
Age in years	64 (46-71)	62 (48-69)	65 (46-71)	.52
Male sex (%)	35 (60)	18 (62)	17 (59)	.79
Race (%)				.25
White	28 (48)	18 (62)	10 (34)	
Black	16 (28)	7 (24)	9 (31)	
Asian	2 (3)	1 (3)	1 (3)	
Other	9 (16)	3 (10)	6 (21)	
Hispanic ethnicity (%)	25 (43)	12 (41)	13 (45)	.79
Organ transplant (%)				.35
Kidney	26 (45)	15 (52)	11 (38)	
Lung	15 (26)	5 (17)	10 (34)	
Liver	2 (3)	1 (3)	1 (3)	
Heart	10 (17)	6 (21)	4 (14)	
Heart-kidney	3 (5)	2 (7)	1 (3)	
Kidney-pancreas	2 (3)	0 (0)	2 (7)	
Comorbidities (%)				
HTN	46 (79)	23 (79)	23 (79)	1
DM	31 (53)	13 (45)	18 (62)	.19
CKD	40 (69)	20 (69)	20 (69)	1
Chronic lung disease	13 (22)	5 (17)	8 (28)	.35
Years from transplant	4.85 (1.42-8.9)	5.77 (2.35-9.69)	4.06 (1.31-7.75)	.51
Baseline immunosuppression (%)				
Calcineurin inhibitor	53 (91)	28 (97)	25 (86)	.16
Mycophenolate	45 (78)	24 (83)	21 (72)	.35
Steroids	41 (71)	22 (76)	19 (66)	.44
Belatacept	3 (5)	1 (3)	2 (7)	.55
Therapy				
Hydroxychloroquine	47 (81)	26 (90)	21 (72)	.10
Azithromycin	32 (55)	16 (55)	16 (55)	.76
Remdesivir	5 (9)	1 (3)	4 (14)	.16
High dose corticosteroids[b]	42 (72)	22 (76)	20 (69)	.88
Disease Severity				
New dialysis requirement	10 (17)	10 (34)	0 (0)	.001
Ever in ICU	26 (45)	18 (62)	8 (28)	.008
Ever Intubated	22 (38)	18 (62)	6 (21)	.003
Secondary complications (%)				
Venous thrombosis	5 (9)	5 (17)	2 (7)	.31
Cerebrovascular events	3 (5)	3 (10)	0 (0)	.10
Patients with infections	17 (29)	10 (34)	7 (24)	.55
Infectious episodes[c]				
Blood stream infection	3 (5)	2 (7)[d]	1 (3)[e]	
Bacterial pneumonia	6 (10)	3 (10)[f]	3 (10)[g]	
C. difficile	1 (2)	1 (3)	1 (3)	
Aspergillus	1 (2)	1 (3)	0 (0)	

(Continues)

Table 1 (Continued)

	All (n = 58)	Tocilizumab group (n = 29)	Matched control group (n = 29)	*P*-value
CMV	10 (17)	5 (17)	5 (17)	
Peak CMV viral load, IU/mL	716 (193-1469)	1469 (1326-8994)	263 (193-418)	
Other infections	2 (3)	2 (7)[h]	0 (0)	
Outcomes				
Death	20 (34)	12 (41)	8 (28)	.27
Hospital discharge	36 (62)	15 (52)	21 (72)	.26

[a]All continuous data presented as median (IQR).
[b]2 patients in control group with unknown steroid status.
[c]Some patients experienced multiple infectious episodes.
[d]*Candida glabrata*, *Klebsiella pneumonia*.
[e]ESBL *Klebsiella pneumonia*.
[f]1 MRSA, 2 *Pseudomonas aeruginosa*.
[g]*Stenotrophomonas maltophilia*, *Burkholderia cepacia* complex, MRSA.
[h]HHV-6, EBV.

C-reactive protein (CRP), D-dimer, ferritin, and procalcitonin prior to and 48 hours after the first dose of tocilizumab are compared. The degree of respiratory support at the time of tocilizumab and at 7 and 28 days of follow-up are reported using an ordinal scale of ambient air/nasal cannula, non-rebreather mask/high flow nasal cannula, and mechanical ventilation. Improvement was defined as requiring less intense forms of oxygen support or discharge from the hospital after tocilizumab treatment.

3 | RESULTS

A total of 117 SOT recipients hospitalized with confirmed SARS-CoV-2 infection were identified, 29 (24.8%) of whom received at least one dose of tocilizumab. Twenty-two patients received one dose of tocilizumab, six patients received two doses, and one patient received three doses. Clinical characteristics and outcomes of the entire cohort are displayed in Table S1. Notably, the overall mortality was significantly higher among patients who received tocilizumab compared to those who did not (41% vs 20%, $P = .03$). In addition, patients who received tocilizumab were also more likely to have received high dose steroids for treatment of COVID-19 (76% vs 24%, $P < .01$).

Given the differences in overall disease severity and treatment approaches between patients who did and did not receive tocilizumab, 29 patients were then selected in a matched control group. There were no differences in baseline characteristics between the groups. While there was no significant difference in mortality (41% vs 28%, $P = .27$) or hospital discharge (52% vs 72%, $P = .26$), tocilizumab was significantly associated with ICU-level care (62% vs 28%, $P = .008$), mechanical ventilation (62% vs 21%, $P = .003$), and new renal replacement therapy (34% vs 0%, $P = .001$; Table 1). The time from COVID-19 diagnosis to death, hospital discharge, or last follow-up was overall 19 days (IQR 9-34) but significantly longer in the tocilizumab group versus the matched control group (22 vs 14 days, $P = .03$).

We then compared outcomes between patients who received the first dose of tocilizumab while mechanically ventilated ($n = 11$) or not ($n = 18$). In this analysis, there were no significant differences in baseline characteristics or outcomes including mortality between these groups (Table 2). Figure 1 depicts the change in oxygen requirement or clinical status (death, hospital discharge) at 7 and 28 days after tocilizumab initiation. By day 28, about 13 (45%) patients experienced clinical improvement, 5 (17%) had no change, 2 (7%) worsened, and 9 (31%) died. Improvement in respiratory status at day 28 was more common among patients who were not intubated (50%) at the time of tocilizumab therapy compared to those who were intubated (36%) at the time of first tocilizumab dose.

Serologic inflammatory markers at baseline and 48 hours after tocilizumab are shown in Table 3. Patients who were intubated had significantly higher baseline levels of CRP and procalcitonin, but not ferritin, D-dimer and IL-6 compared to nonintubated patients. These differences remained significant for 48 hours from first dose of tocilizumab. As expected, IL-6 levels dramatically increased after tocilizumab administration.

4 | DISCUSSION

There is an urgent need to better define effective and safe therapies to reduce morbidity and mortality associated with COVID-19, in particular for the hyperinflammatory phase. While remdesivir and dexamethasone have been shown to reduce mortality among selected patients with COVID-19, the benefit of other therapeutic interventions remains inconclusive for not only the general population but also for SOT recipients. Here we present a retrospective matched cohort study on the use of off-label tocilizumab for SOT recipients hospitalized due to COVID-19. In this population, the

TABLE 2 Clinical characteristics and outcomes of SOT recipients with COVID-19 who received tocilizumab prior to or following endotracheal intubation[a]

	All tocilizumab patients (n = 29)	Nonintubated (n = 18)	Intubated (n = 11)	*P*-value
Age in years	62 (48-69)	63 (51-68)	61 (40-71)	.91
Male sex (%)	18 (62)	12 (67)	6 (55)	.51
Race (%)				.84
White	18 (62)	11 (61)	7 (64)	
Black	7 (24)	4 (22)	3 (27)	
Asian	1 (3)	1 (6)	0 (0)	
Other	3 (10)	2 (11)	1 (9)	
Hispanic ethnicity (%)	12 (41)	7 (39)	5 (45)	.73
Organ transplant (%)				.43
Kidney	15 (52)	7 (39)	8 (73)	
Lung	5 (17)	4 (22)	1 (9)	
Liver	1 (3)	1 (6)	0 (0)	
Heart	6 (21)	5 (28)	1 (9)	
Heart-kidney	2 (7)	1 (6)	1 (9)	
Comorbidities (%)				
HTN	22 (76)	14 (78)	8 (73)	.76
DM	13 (45)	8 (44)	5 (45)	.96
CKD	20 (69)	12 (67)	8 (73)	.73
Chronic lung disease	5 (17)	3 (17)	2 (18)	.92
Years from transplant	5.77 (2.35-9.69)	5.97 (2.45-9.69)	5.77 (1.26-10.02)	.67
Baseline immunosuppression (%)				
Calcineurin inhibitor	28 (97)	18 (100)	10 (91)	.19
Mycophenolate	24 (83)	16 (89)	8 (73)	.26
Steroids	22 (76)	14 (78)	8 (73)	.71
Belatacept	1 (3)	0 (0)	1 (9)	.19
IVIG +/- Pheresis	4 (14)	3 (17)	1 (9)	.57
Thymoglobulin	4 (14)	2 (11)	2 (18)	.59
Therapy				
Hydroxychloroquine	26 (90)	15 (83)	11 (100)	.15
Azithromycin	16 (55)	9 (50)	7 (64)	.70
Remdesivir	1 (3)	1 (6)	0 (0)	.43
High dose corticosteroids	22 (76)	15 (83)	7 (64)	.23
Days from				
Diagnosis to tocilizumab	9 (4-12)	10 (3-13)	9 (4-11)	.75
Diagnosis to death/ discharge/last f/u	22 (15-44)	22 (15-28)	29 (16-70)	.19
Disease severity				
New dialysis requirement	10 (34)	5 (28)	5 (45)	.33
Ever in ICU	18 (62)	7 (39)	11 (100)	.001
Ever intubated	18 (62)	7 (39)	11 (100)	.001
Secondary complications (%)				
Venous thrombosis	5 (17)	3 (17)	2 (18)	.92
Cerebrovascular events	3 (10)	2 (11)	1 (0)	.86
Patients with infections[b]	10 (34)	5 (28)	5 (45)	.39

(Continues)

Table 2 (Continued)

	All tocilizumab patients (n = 29)	Nonintubated (n = 18)	Intubated (n = 11)	*P*-value
Outcomes				
Death	12 (41)	7 (39)	5 (45)	.73
Hospital discharge	15 (52)	10 (56)	5 (45)	.54

[a]All continuous data presented as median (IQR).

[b]2 patients experienced multiple infectious episodes.

			Oxygen support needed at time of first dose of tocilizumab			
			Mechanical ventilation (n=11)	NRB/HFNC (n=11)	Nasal Cannula (n=6)	Ambient Air (n=1)
Oxygen support needed or clinical status after tocilizumab	Day 7	Deceased	2	0	0	0
		Mechanical ventilation	8	6	0	0
		NRB/HFNC	0	2	0	0
		Nasal Cannula	1	2	3	0
		Ambient Air	0	0	0	0
		Discharged	0	1	3	1
		Improved	9%	27%	50%	100%
	Day 28	Deceased*	4	5	0	0
		Mechanical ventilation	3	2	0	0
		NRB/HFNC	0	1	0	0
		Nasal Cannula	2	1	1	0
		Ambient Air	0	1	0	0
		Discharged	2	1	5	1
		Improved	36%	27%	83%	100%

FIGURE 1 Clinical status or change in oxygen requirement 7 and 28 d after treatment with tocilizumab (Color scheme: red = worsening, yellow = no change, green = improvement). *3 patients died >28 d after first tocilizumab dose and are not included here [Color figure can be viewed at wileyonlinelibrary.com]

overall mortality was 26% but up to 41% among those with more severe disease leading to use of tocilizumab. When matched for severe COVID-19 risk factors (age, hypertension, and CKD) as well as high dose corticosteroids, there was no significant difference in mortality between patients who received tocilizumab and matched controls. However, despite matching, patients who received tocilizumab were more likely to be in the ICU, mechanically ventilated, and on new renal replacement therapy, and had a longer overall length of stay, likely indicating more severe disease overall. In addition, while there was no difference in mortality based on level of oxygen support required at time of tocilizumab initiation (intubated vs not intubated), patients who were not intubated at the time of this treatment were more likely to show clinical improvement by day 28 of follow-up.

The use of tocilizumab in SOT recipients with severe COVID-19 has been previously reported, including a multicenter cohort study from Spain.[20–25] In that study of 80 kidney transplant recipients treated with tocilizumab for severe COVID-19, mortality was higher than the comparator group (32.5% vs 21.9%), but the authors suggest that this difference could potentially have been more pronounced due to a more critically ill tocilizumab group. Although reporting on a larger cohort, the unmatched design of the study limits any significant conclusions. In contrast, our matched comparison showed no significant beneficial response from tocilizumab. This seems to be in line with the recent termination of phase 3 studies for the IL-6 receptor inhibitors tocilizumab and sarilumab, both due to not achieving primary and key secondary endpoints. However, it remains unknown whether there are certain populations including those with indicators of a hyperimmune response, may derive benefit in some circumstances.

Although secondary infections occurred in over one-third of patients receiving tocilizumab, including a relatively high rate of CMV reactivation (17%), this was not significantly higher than the matched control group. This suggests that the impact of tocilizumab on the net state of immunosuppression among already chronically immunosuppressed SOT recipients may be limited and less significant than concurrent high dose steroid administration or critical illness in these patients. Similarly, there were no differences in other complications such as venous thrombosis or cerebrovascular events and no cases of bowel perforation. These results suggest that tocilizumab administration appears to be safe overall, which is consistent with prior reports among both SOT and non-SOT patients with COVID-19.

Assessment of COVID-19 disease severity and response to immunomodulatory therapy through inflammatory markers has been

TABLE 3 Inflammatory markers before and after tocilizumab by baseline respiratory status

	All (n = 29)	Nonintubated (n = 18)	Intubated (n = 11)	*P*-value
Biomarker levels				
CRP, mg/L				
Baseline	151 (51-204)	102.6 (27.9-155)	203.5 (157-252.1)	.01
48 hrs after tocilizumab	50.49 (10.11-123.35)	15.58 (5.07-66)	133.45 (96.25-163)	.005
Ferritin, ng/ml				
Baseline	1240 (696-2216)	1386 (661.2-2774)	1215 (840-1968)	.78
48 hrs	1359 (690.7-2880.5)	1395.5 (645.4-3137)	1186 (736-2067)	.68
D-Dimer, ug/m				
Baseline	2.69 (1.08-7.8)	2.29 (1-3.38)	4.98 (2.47-9)	.12
48 hrs	3.67 (1.77-8.18)	3.48 (1.68-5.46)	5.48 (3.33-8.54)	.47
Procalcitonin, ng/ml				
Baseline	0.385 (0.16-1.92)	0.19 (0.12-1.37)	1 (0.43-2.36)	.02
48 hrs	0.7 (0.12-1.4)	0.14 (0.09-0.97)	1.24 (0.51-3.27)	.04
IL−6, pg/ml				
Baseline	55.5 (18-183.5)	31.1 (16-84.2)	102.7 (33-225.2)	.15
48 hrs	>315	>315	>315	—

widely reported. In our cohort, serum CRP and procalcitonin levels were significantly higher in those requiring mechanical ventilation at the time of tocilizumab administration, a difference that remained significant 48 hours later. Unlike other studies, a downtrend in CRP levels after tocilizumab did not correlate with clinical improvement in our study (data not shown).

There are several limitations in this study. The modest number of cases and controls included limit the ability to detect small to moderate differences in outcomes. Secondly, despite matching for key characteristics known to impact disease severity as well as the use of concomitant high dose corticosteroids, the fact that patients who received tocilizumab were more likely to require new renal replacement therapy, mechanical ventilation, or be admitted to an ICU raises the possibility that those patients had more severe disease than the matched control group. As patients received tocilizumab treatment at variable times in their disease progression, matching for disease severity in this cohort was not possible. Finally, a potential limitation to this analysis is the possibility that SOT patients who received tocilizumab may have presented earlier in the pandemic and thus did not benefit from improvements in care that occurred in subsequent months.

In summary, administration of tocilizumab for treatment of severe COVID-19 among SOT recipients appeared to be safe but was not associated with reduced mortality in this matched cohort study. Further studies on the safety, efficacy, and optimal timing of tocilizumab in immunocompromised patients are warranted.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Marcus R. Pereira https://orcid.org/0000-0002-9214-9122
Meghan M. Aversa https://orcid.org/0000-0002-7361-0024
Maryjane A. Farr https://orcid.org/0000-0003-1066-9368
Benjamin A. Miko https://orcid.org/0000-0002-6115-3014
Justin G. Aaron https://orcid.org/0000-0003-1732-7870
Sumit Mohan https://orcid.org/0000-0002-5305-9685
Syed A. Husain https://orcid.org/0000-0002-1823-0117
Nir Uriel https://orcid.org/0000-0003-2301-3587
Elizabeth X. Zheng https://orcid.org/0000-0001-6428-5525
Alyson N. Fox https://orcid.org/0000-0003-0398-4589
Demetra S. Tsapepas https://orcid.org/0000-0001-6428-5525
Elizabeth C. Verna https://orcid.org/0000-0002-9658-3751

REFERENCES

1. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: Initial report from the US epicenter. *Am J Transplant*. 2020;20(7):1800–1808.
2. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382:2475–2477.
3. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. *Kidney Int*. 2020;97(6):1076–1082.
4. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant*. 2020;20(7):1819–1825.
5. Latif F, Farr MA, Clerkin KJ, et al. Characteristics and outcomes of recipients of heart transplant with coronavirus disease 2019. *JAMA Cardiol*. 2020. https://doi.org/10.1001/jamacardio.2020.2159

6. Chaudhry ZS, Williams JD, Vahia A, et al. Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: a cohort study. *Am J Transplant*. 2020. https://doi.org/10.1111/ajt.16188
7. Kates OS, Haydel BM, Florman SS, et al. COVID-19 in solid organ transplant: A multi-center cohort study. *Clin Infect Dis*. 2020. https://doi.org/10.1093/cid/ciaa1097
8. Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe Covid-19. *N Engl J Med*. 2020;382(24):2327–2336.
9. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19–preliminary report. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMoa2007764
10. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. The cytokine release syndrome (CRS) of severe COVID-19 and Interleukin-6 receptor (IL-6R) antagonist Tocilizumab may be the key to reduce the mortality. *Int J Antimicrob Agents*. 2020;105954.
11. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395:1033–1034.
12. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19–preliminary report. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMoa2021436
13. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: A single center experience. *J Med Virol*. 2020;92(7):814–818. https://doi.org/10.1002/jmv.25801
14. Xu X, Han M, Li T, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci USA*. 2020;117(20):10970–10975.
15. Guaraldi G, Meschiari M, Cozzi-Lepri A, et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. *Lancet Rheumatol*. 2020;2:e474–e484.
16. Sanofi and Regeneron provide update on Kevzara® (sarilumab) Phase 3 U.S. trial in COVID-19 patients. 2020. https://www.sanofi.com/en/media-room/press-releases/2020/2020-07-02-22-30-00 Accessed August 27, 2020.
17. Roche provides an update on the phase III COVACTA trial of Actemra/RoActemra in hospitalised patients with severe COVID-19 associated pneumonia. 2020. https://www.roche.com/investors/updates/inv-update-2020-07-29.htm Accessed August 27, 2020.
18. Jordan SC, Choi J, Kim I, et al. Interleukin-6, A Cytokine Critical to Mediation of Inflammation, Autoimmunity and Allograft Rejection: Therapeutic Implications of IL-6 Receptor Blockade. *Transplantation*. 2017;101:32–44.
19. Choi J, Aubert O, Vo A, et al. Assessment of Tocilizumab (Anti-Interleukin-6 Receptor Monoclonal) as a Potential Treatment for Chronic Antibody-Mediated Rejection and Transplant Glomerulopathy in HLA-Sensitized Renal Allograft Recipients. *Am J Transplant*. 2017;17:2381–2389.
20. Faguer S, Del Bello A, Abravanel F, Nicolau-Travers ML, Kamar N. Tocilizumab for Hemophagocytic Syndrome in a Kidney Transplant Recipient With COVID-19. *Ann Intern Med*. 2020;173(6):501–503.
21. Fontana F, Alfano G, Mori G, et al. COVID-19 pneumonia in a kidney transplant recipient successfully treated with tocilizumab and hydroxychloroquine. *Am J Transplant*. 2020;20(7):1902–1906.
22. Hammami MB, Garibaldi B, Shah P, et al. Clinical Course of COVID-19 in a Liver Transplant Recipient on Hemodialysis and Response to Tocilizumab Therapy: A Case Report. *Am J Transplant*. 2020;20(8):2254–2259.
23. Holzhauser L, Lourenco L, Sarswat N, Kim G, Chung B, Nguyen AB. Early experience of COVID-19 in 2 heart transplant recipients: case reports and review of treatment options. *Am J Transplant*. 2020;20(10):2916–2922.
24. Perez-Saez MJ, Blasco M, Redondo-Pachon D, et al. Use of tocilizumab in kidney transplant recipients with COVID-19. *Am J Transplant*. 2020. https://doi.org/10.1111/ajt.16192
25. Morillas JA, Marco Canosa F, Srinivas P, et al. Tocilizumab therapy in five solid and composite tissue transplant recipients with early ARDS due to SARS-CoV-2. *Am J Transplant*. 2020. https://doi.org/10.1111/ajt.16080

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Pereira MR, Aversa MM, Farr MA, et al. Tocilizumab for severe COVID-19 in solid organ transplant recipients: a matched cohort study. *Am. J. Transplant*. 2020;20:3198–3205. https://doi.org/10.1111/ajt.16314