Supplementary Appendix

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Supplementary Methods

Supplementary Methods 1. Tocilizumab usage criteria for COVID-19 at Michigan Medicine during the study period.

| Tocilizumab ID APPROVAL NEEDED | **Dose rounding currently built into Epic order. Doses should be rounded to nearest available full vial (80 mg, 200 mg, 400 mg vials)** |
|--------------------------------|--------------------------------------------------------------------------------------------------|
| **May be considered for a patient meeting all criteria (#1-#6) below and is not eligible for the sarilumab trial or cannot receive sarilumab in a timely fashion.** | **Laboratory Parameters also supportive of cytokine storm:** |
| Based on available data, the evidence for benefit is weak, and a risk for potential harm exists (possible risk of infection). | • Ferritin >300 ug/L (or surrogate) with doubling within 24 hours |
| 1. COVID-19 positive | • Ferritin >600 ug/L at presentation and LDH >250 U/L |
| 2. All of the following respiratory findings: | • Elevated D-dimer (>1 mg/L) |
| a. Abnormal chest imaging consistent with COVID-19 | **Serious adverse events:** |
| b. Rapidly worsening gas exchange/respiratory status over 24-48 hours and requiring ≥4-6 L/min O₂ | • Gastrointestinal perforation |
| 3. Absence of systemic bacterial or fungal co-infection | • Anemia |
| 4. High clinical suspicion for cytokine release syndrome supported by elevated inflammatory markers (e.g., ferritin >600 ug/mL; D-dimer >1.0 mg/L) and clinical decline. | • Hepatitis |
| 5. Does not have a poor prognosis where they are unlikely to survive >48 hours | • Infusion reaction |
| 6. Mechanical ventilation for ≤48 hours | • Neutropenia |
| **Duration:** One dose | **Infection** |

Adult Dosing (≥18 years):
8 mg/kg (max: 800 mg/dose)

Pediatric Dosing (<18 years):
- <30 kg:
  - 12 mg/kg
- ≥30 kg:
  - 8 mg/kg
  - (max: 800 mg/dose)

There are no data to inform risk vs benefit of a second dose 48-72 hours later. Based on local experience a second dose is rarely needed and administration of a second dose should not be routine practice.
Supplementary Figures

Figure S1. Propensity score model diagnostics.
The propensity score included the following variables: age, congestive heart failure, chronic pulmonary disease, chronic renal disease, therapeutic anticoagulation, ferritin, LDH, AST. The model was constructed based on the cohort subset with complete data (n=116); excluded patients were missing at least one of the following laboratory values: ferritin, LDH, and/or AST.

Figure S1A. Area under the ROC curve (AU-ROC).
This figure illustrates the prediction ability of our propensity score model with an AU-ROC of 70.1%.

Figure S1B. Distribution of propensity scores across patients with and without tocilizumab treatment.
The propensity score distributions demonstrate a reasonably good overlap between the two treatment groups.
**Figure S2. Inverse probability of treatment weighted Kaplan Meier curve of survival (n=116)**

Time from intubation to death or censoring. Limited to patients with complete data for variables included in the propensity score model. Propensity score estimates were based on age, congestive heart failure, chronic pulmonary disease, chronic renal disease, therapeutic anticoagulation, ferritin, LDH, and AST (model shown in Table S3). Complete data were available for all cohort patients for demographics, comorbidity and treatments. Excluded patients were missing at least one of the following laboratory values: ferritin, LDH, and/or AST. Curves are weighted by inverse probability of treatment group (IPTW) based on the propensity score model shown in Table S3 (i.e., for tocilizumab-treated patients, IPTW=1/(propensity score); for untreated patients, IPTW=1/(1-propensity score)). Unadjusted IPTW hazard ratio for tocilizumab treated vs. untreated from corresponding Cox proportional hazards model: HR 0.55 [95% CI 0.34, 0.90]; \( p = 0.02 \).
Figure S3. Hazard ratio estimates of the association between tocilizumab and survival.
Time from intubation to death or censoring. All hazard ratio estimates are for tocilizumab (treated vs. untreated) for the model specified. Full model results, including hazard ratios for other covariates in multivariable models, are shown in Table S6. Magnitude and direction of association between tocilizumab and outcome remained similar in each of the bivariable models, as well as the multivariable models.

| Model                                      | Estimate [95% CI] | N  |
|--------------------------------------------|-------------------|----|
| Unadjusted                                 | 0.50 [0.27, 0.90] | 154|
| Male-only                                  | 0.53 [0.26, 1.06] | 102|
| Female-only                                | 0.41 [0.13, 1.33] | 52 |
| Age <70-only                                | 0.55 [0.27, 1.13] | 122|
| Age >75-only                                | 0.57 [0.29, 1.10] | 137|
| Age 60-less only                           | 0.59 [0.21, 1.72] | 76 |
| Non-transfer-only                          | 0.41 [0.15, 1.11] | 53 |
| Transfer-only                              | 0.54 [0.25, 1.15] | 101|
| CRP >150 only                              | 0.48 [0.21, 1.11] | 90 |
| D-Dimer 1.2 only                           | 0.42 [0.19, 0.94] | 104|
| Anticoag treated only                      | 0.56 [0.20, 0.94] | 109|
| Anticoag untreated only                    | 0.24 [0.05, 0.98] | 45 |
| Age-adjusted                               | 0.55 [0.29, 1.01] | 154|
| Sex-adjusted                               | 0.49 [0.27, 0.89] | 154|
| Race-adjusted                              | 0.49 [0.27, 0.89] | 154|
| Ethnic-adjusted                            | 0.52 [0.26, 0.94] | 154|
| BMI-adjusted                               | 0.50 [0.27, 0.91] | 154|
| Hypertension-adjusted                      | 0.50 [0.27, 0.90] | 154|
| Congestive heart failure-adjusted          | 0.50 [0.28, 0.93] | 154|
| Chronic pulmonary disease-adjusted         | 0.53 [0.29, 0.98] | 154|
| Asthma-adjusted                            | 0.49 [0.27, 0.90] | 154|
| Sleep apnea-adjusted                       | 0.51 [0.28, 0.93] | 154|
| Diabetes-adjusted                          | 0.51 [0.28, 0.93] | 154|
| Renal disease-adjusted                     | 0.51 [0.28, 0.94] | 154|
| Transfer-adjusted                          | 0.49 [0.26, 0.89] | 154|
| Time to Vent-adjusted                      | 0.50 [0.27, 0.91] | 154|
| HCO-adjusted                               | 0.48 [0.26, 0.88] | 154|
| Anticoag-adjusted                          | 0.48 [0.26, 0.88] | 154|
| Methylprednisolone-adjusted                | 0.49 [0.27, 0.89] | 154|
| Progesterone-adjusted                      | 0.52 [0.28, 0.96] | 154|
| Temperature-adjusted                       | 0.39 [0.20, 0.80] | 144|
| Albumin-adjusted                           | 0.46 [0.22, 0.95] | 141|
| ALC-adjusted                               | 0.38 [0.18, 0.80] | 121|
| ALT-adjusted                               | 0.48 [0.24, 0.99] | 140|
| AST-adjusted                               | 0.46 [0.24, 0.99] | 140|
| CRP-adjusted                               | 0.40 [0.20, 0.81] | 135|
| D-Dimer-adjusted                           | 0.36 [0.17, 0.78] | 129|
| Ferritin-adjusted                          | 0.48 [0.24, 0.99] | 129|
| LDH-adjusted                               | 0.37 [0.17, 0.80] | 123|
| WBC-adjusted                               | 0.41 [0.21, 0.82] | 142|
| PaO2/FIO2-adjusted                         | 0.34 [0.14, 0.84] | 80 |
| Demographic-adjusted                      | 0.54 [0.29, 1.00] | 154|
| IPTW                                       | 0.58 [0.34, 0.99] | 116|
| IPTW/Demographic-adjusted/MI               | 0.55 [0.33, 0.90] | 116|
| IPTW/Demographic-adjusted/Multiple-imputation | 0.54 [0.35, 0.84] | 154 |

- Demographic-adjusted=controlled for age, sex, and race as covariates
- IPTW=weighted by inverse probability of treatment group, based on the propensity score model shown in Table S3
- MI=multiple imputation, used to impute missing laboratory values as relevant for ferritin, LDH, and/or AST. Twenty-five imputations by fully conditional specification were made based on age, sex, race, ethnicity, transfer status, history of hypertension, congestive heart failure, chronic pulmonary disease, and chronic renal disease.
Figure S4. Odds ratio estimates of the association between tocilizumab and clinical status (ordinal outcome) on Day 28.

Odds ratio estimates from proportional odds models, using 6-level ordinal outcome for illness severity, incorporating superinfection occurrence (see key for levels). Lower odds ratios are “favorable” (i.e., indicate decreased likelihood of worse outcomes). Full model results, including odds ratios for other covariates in multivariable models, are shown in Table S7.

Univariate

Stratum-specific sensitivity analyses

6-level ordinal outcome:
1. Discharged alive
2. Hospitalized, off vent, no superinfection
3. Hospitalized, off vent, with superinfection
4. Hospitalized, mechanically ventilated, no superinfection
5. Hospitalized, mechanically ventilated, with superinfection
6. Death

Bivariable models

Multivariable models

*a Demographic-adjusted=controlled for age, sex, and race as covariates

b IPTW=weighted by inverse probability of treatment group, based on the propensity score model shown in Table S3

c MI=multiple imputation, used to impute missing laboratory values as relevant for ferritin, LDH, and/or AST. Twenty-five imputations by fully conditional specification were made based on age, sex, race, ethnicity, transfer status, history of hypertension, congestive heart failure, chronic pulmonary disease, and chronic renal disease.

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Table S1. Unadjusted Cox proportional hazards models of survival.  
Time from intubation to death or censoring.

| Model | Hazard Ratio [95% CI] | p-value | n  |
|-------|-----------------------|---------|----|
| Tocilizumab: (treated vs. not-treated) | 0.50 [0.27, 0.90] | 0.02 | 154 |
| Age (per 10 years) | 1.44 [1.16, 1.79] | 0.001 | 154 |
| Male vs. female | 1.36 [0.71, 2.58] | 0.35 | 154 |
| Race: Black vs. white | 0.81 [0.40, 1.61] | 0.55 | 154 |
| Race: Other vs. white | 1.23 [0.56, 2.69] | 0.61 | 154 |
| Ethnicity: Hispanic vs. non-Hispanic | --- | --- | 154 |
| BMI (per 5 kg/m²) | 0.92 [0.78, 1.07] | 0.28 | 154 |
| Hypertension (yes vs. no) | 1.24 [0.66, 2.32] | 0.51 | 154 |
| Congestive heart failure (yes vs. no) | 2.20 [1.21, 4.00] | 0.01 | 154 |
| Chronic pulmonary disease (yes vs. no) | 1.74 [0.90, 3.36] | 0.10 | 154 |
| Asthma (yes vs. no) | 1.59 [0.82, 3.07] | 0.17 | 154 |
| Sleep apnea (yes vs. no) | 1.41 [0.76, 2.61] | 0.28 | 154 |
| Diabetes (yes vs. no) | 1.61 [0.80, 3.24] | 0.18 | 154 |
| Renal disease (yes vs. no) | 1.44 [0.81, 2.57] | 0.21 | 154 |
| Transfer patient (Yes vs. no) | 1.00 [0.55, 1.84] | 1.00 | 154 |
| Days from admit to vent | 0.96 [0.82, 1.13] | 0.66 | 154 |
| HCQ: (treated vs. not-treated) | 1.33 [0.70, 2.54] | 0.38 | 154 |
| Therapeutic anticoag: (treated vs. not-treated) | 1.27 [0.66, 2.45] | 0.48 | 154 |
| Methylprednisolone: (treated vs. not-treated) | 1.30 [0.62, 2.68] | 0.49 | 154 |
| Prone positioning: (yes vs. no) | 0.60 [0.28, 1.29] | 0.19 | 154 |
| Temperature: (at admission per °F) | 1.13 [0.96, 1.34] | 0.15 | 144 |
| Albumin: (per g/dL) | 0.64 [0.35, 1.17] | 0.15 | 141 |
| ALC: (per 10⁹/L) | 0.50 [0.21, 1.18] | 0.11 | 121 |
| ALT: (per 10 g/dL) | 1.01 [1.00, 1.01] | 0.15 | 140 |
| AST: (per 10 g/dL) | 1.01 [1.00, 1.01] | 0.005 | 140 |
| CRP: (per 100 g/L) | 0.66 [0.13, 3.23] | 0.60 | 135 |
| D-Dimer: (per 10 g/dL) | 1.19 [0.93, 1.54] | 0.17 | 129 |
| Ferritin: (per 1000 g/dL) | 1.17 [1.05, 1.30] | 0.003 | 129 |
| LDH: (per 100 U/L) | 1.10 [1.04, 1.15] | <0.001 | 123 |
| WBC: (per 10⁹/L) | 1.02 [0.97, 1.07] | 0.51 | 142 |
| PaO2/FiO2: (per 10) | 1.01 [0.94, 1.08] | 0.89 | 80 |

*Hazard ratio estimates undefined (no deaths among n=3 patients of Hispanic ethnicity)*
Table S2. Unadjusted proportional odds model results of clinical status (ordinal outcome) at Day 28.
Odds ratio (OR) estimates from proportional odds models represent OR per 1 level increase in the six-level ordinal outcome scale for illness severity, including superinfections (see key for levels). Lower odds ratios are “favorable” (i.e., indicate decreased likelihood of worse outcomes).

| Model                                                                 | Odds Ratio [95% CI]     | p-value | n  |
|----------------------------------------------------------------------|------------------------|---------|----|
| Tocilizumab: (treated vs. not-treated)                               | 0.57 [0.32, 1.01]       | 0.05    | 154|
| Age (per 10 years)                                                   | 1.20 [0.99, 1.46]       | 0.06    | 154|
| Male vs. female                                                      | 1.27 [0.70, 2.32]       | 0.43    | 154|
| Race: Black vs. white                                                | 0.87 [0.59, 1.27]       | 0.47    | 154|
| Race: Other vs. white                                                | 1.18 [0.74, 1.88]       | 0.50    | 154|
| Ethnicity: Hispanic vs. non-Hispanic                                 | 0.53 [0.06, 4.36]       | 0.55    | 154|
| BMI (per 5 kg/m²)                                                    | 0.90 [0.77, 1.04]       | 0.16    | 154|
| Hypertension (yes vs. no)                                            | 1.10 [0.60, 2.00]       | 0.76    | 154|
| Congestive heart failure (yes vs. no)                                | 1.57 [0.81, 3.08]       | 0.18    | 154|
| Chronic pulmonary disease (yes vs. no)                               | 1.49 [0.72, 3.07]       | 0.28    | 154|
| Asthma (yes vs. no)                                                  | 1.97 [0.97, 4.02]       | 0.06    | 154|
| Sleep apnea (yes vs. no)                                             | 1.05 [0.55, 1.98]       | 0.89    | 154|
| Diabetes (yes vs. no)                                                | 1.32 [0.61, 2.84]       | 0.48    | 154|
| Renal disease (yes vs. no)                                           | 1.69 [0.95, 3.01]       | 0.08    | 154|
| Transfer patient (Yes vs. no)                                        | 1.33 [0.73, 2.42]       | 0.35    | 154|
| Days from admit to vent                                              | 1.00 [0.86, 1.15]       | 0.95    | 154|
| HCQ: (treated vs. not-treated)                                       | 0.99 [0.51, 1.95]       | 0.98    | 154|
| Therapeutic anticoag: (treated vs. not)                              | 2.26 [1.19, 4.28]       | 0.01    | 154|
| Methylprednisolone: (treated vs. not)                                | 2.49 [1.12, 5.52]       | 0.02    | 154|
| Prone positioning: (yes vs. no)                                     | 1.13 [0.58, 2.20]       | 0.72    | 154|
| Temperature: (at admission per F)                                   | 1.09 [0.93, 1.29]       | 0.29    | 144|
| Albumin: (per g/dL)                                                  | 0.58 [0.31, 1.07]       | 0.08    | 141|
| ALC: (per 10⁷/L)                                                     | 0.57 [0.26, 1.25]       | 0.16    | 121|
| ALT: (per 10 g/dL)                                                   | 1.00 [0.99, 1.02]       | 0.36    | 140|
| AST: (per 10 g/dL)                                                   | 1.01 [0.99, 1.02]       | 0.32    | 140|
| Bilirubin: (per g/dL)                                                | 1.10 [0.72, 1.68]       | 0.65    | 140|
| CRP: (per 100 g/L)                                                   | 1.01 [0.94, 1.08]       | 0.83    | 135|
| D-Dimer: (per 10 g/dL)                                               | 1.26 [0.95, 1.66]       | 0.10    | 129|
| Ferritin: (per 1000 g/dL)                                            | 1.22 [1.04, 1.42]       | 0.01    | 129|
| LDH: (per 100 U/L)                                                   | 1.08 [1.00, 1.17]       | 0.05    | 123|
| WBC: (per 10⁹/L)                                                     | 1.02 [0.97, 1.06]       | 0.47    | 142|
| Pao2/FiO2: (per 10)                                                  | 0.97 [0.90, 1.04]       | 0.41    | 80 |

6-level ordinal outcome:
(1) Discharged alive
(2) Hospitalized, off vent, no superinfection
(3) Hospitalized, off vent, with superinfection
(4) Hospitalized, mechanically ventilated, no superinfection
(5) Hospitalized, mechanically ventilated, with superinfection
(6) Death
**Table S3. Propensity score model for tocilizumab treatment (n=116).**

Results of binary logistic regression model with outcome=treated vs. untreated with tocilizumab. Limited to patients with complete data for variables included. There were no missing demographic, comorbidity or treatment data. Excluded patients were missing at least one of the following labs: ferritin, LDH, and/or AST.

| Model                                              | Odds Ratio [95% CI] | p-value |
|----------------------------------------------------|---------------------|---------|
| Age (per 10 years)                                 | 0.77 [0.58, 1.02]   | 0.06    |
| Congestive heart failure (yes vs. no)              | 1.26 [0.41, 3.88]   | 0.69    |
| Chronic pulmonary disease (yes vs. no)             | 0.37 [0.11, 1.20]   | 0.10    |
| Chronic renal disease (yes vs. no)                 | 0.68 [0.28, 1.64]   | 0.38    |
| Therapeutic anticoag: (treated vs. not-treated)    | 1.78 [0.69, 4.58]   | 0.23    |
| Ferritin: (per 1000 g/dL)                          | 0.97 [0.78, 1.20]   | 0.77    |
| LDH: (per 100 U/L)                                 | 1.08 [0.93, 1.24]   | 0.33    |
| AST: (per 10 g/dL)                                 | 0.98 [0.92, 1.04]   | 0.47    |

**Table S4. Balancing after inverse probability of treatment weighting (n=116)**

Limited to patients with complete data for variables included. Pre-IPTW reflects the unadjusted distributions between tocilizumab-treated and untreated patients; post-IPTW are distributions after weighting each patient by the inverse probability of treatment group based on the propensity score model shown in **Table S3**. (i.e., for tocilizumab-treated patients, IPTW=1/(propensity score); for untreated patients, IPTW=1/(1-propensity score).

| Characteristic                        | Pre-IPTW        | Post-IPTW       | p-value |
|---------------------------------------|-----------------|-----------------|---------|
|                                       | tocilizumab-    | tocilizumab-    |         |
|                                       | treated         | untreated       |         |
| Age, Mean (SD)                        | 53 (16.0)       | 61 (14.2)       | <0.001  |
| Congestive heart failure, %           | 16              | 25              | 0.24    |
| Chronic pulmonary disease, %          | 10              | 27              | 0.03    |
| Chronic renal disease, %              | 35              | 49              | 0.12    |
| Therapeutic anticoagulation, %        | 82              | 68              | 0.08    |
| Ferritin, Mean (SD)                   | 1854 (2525)     | 2199 (2513)     | 0.47    |
| LDH, Mean (SD)                        | 746 (403)       | 712 (569)       | 0.78    |
| AST, Mean (SD)                        | 101 (88)        | 183 (652)       | 0.38    |
Table S5. Comparison of patients included and excluded from IPTW model based on missing lab data.
Limited to 116 patients with complete data for variables included. Propensity score estimates based on age, congestive heart failure, chronic pulmonary disease, chronic renal disease, therapeutic anticoag, ferritin, LDH, and AST (model shown in Table S3). There were no missing demographic, comorbidity or treatment data. Excluded patients were missing at least one of the following labs: ferritin, LDH, and/or AST.

| Baseline characteristics | Included in propensity score analysis (n=116) | Not included in propensity score analysis (n=38) | p-value |
|--------------------------|---------------------------------------------|-----------------------------------------------|---------|
| Age*                     | 58 (15.2)                                   | 58 (13.8)                                    | 0.95    |
| Female                   | 39 (34)                                     | 13 (34)                                      |         |
| Race                     |                                             |                                              | 0.61    |
| Black                    | 62 (53)                                     | 19 (50)                                      |         |
| White                    | 32 (28)                                     | 9 (24)                                       |         |
| Other/Unknown            | 22 (19)                                     | 10 (26)                                      |         |
| Weight (kg)              | 96 (25.5)                                   | 106 (35.6)                                   | 0.12    |
| BMI (kg/m^2)*            | 33.2 (9.07)                                 | 36.8 (10.35)                                 | 0.05    |
| National Early Warning Score (NEWS)^+ (n=61) | 7 (4 to 8) (n=42) | 7 (4 to 7) (n=19) | 0.26    |
| Outside Hospital transfer| 81 (70)                                     | 20 (53)                                      | 0.05    |
| Transfer on mechanical ventilation | 59 (51) | 15 (39) | 0.22    |

| Comorbid conditions      |                                             |                                              |         |
| Hypertension             | 75 (65)                                     | 27 (71)                                      | 0.47    |
| Congestive heart failure | 25 (22)                                     | 11 (29)                                      | 0.35    |
| Chronic pulmonary disease** | 23 (20)                     | 6 (16)                                       | 0.58    |
| Asthma                   | 23 (20)                                     | 8 (21)                                       | 0.87    |
| Sleep apnea              | 31 (27)                                     | 10 (26)                                      | 0.96    |
| Diabetes                 | 19 (16)                                     | 6 (16)                                       | 0.93    |
| Chronic kidney disease   | 50 (43)                                     | 14 (37)                                      | 0.50    |
| Chronic liver disease    | 1 (1)                                       | 1 (3)                                        | 0.40    |
| Solid organ transplant   | 5 (4)                                       | 4 (11)                                       | 0.16    |
| Temperature* °Fahrenheit | 100.4 (1.75)                                | 100.6 (1.89)                                 | 0.74    |

| Laboratory values at time of intubation (with corresponding sample sizes due to missing data) |
|---------------------------------------------|---------------------------------------------|-----------------------------------------------|
| PaO2/FiO2^# (n=69)                          | 165 (139.0 to 230.0) (n=57)                 | 165 (132.0 to 240.0) (n=23)                   | 0.97    |
| White blood cell count^ (10⁹/L) (n=142)     | 13.4 (6.69) (n=115)                         | 12.0 (5.35) (n=27)                           | 0.31    |
| Absolute lymphocyte count^ (10⁹/L) (n=121)  | 0.8 (0.41) (n=102)                         | 0.8 (0.51) (n=19)                           | 0.83    |
| Albumin* (g/dL) (n=141)                     | 3.2 (0.49) (n=116)                         | 3.4 (0.46) (n=25)                           | 0.17    |
| C-reactive protein^ (mg/L) (n=135)          | 22 (14 to 30) (n=114)                      | 15 (9 to 23) (n=21)                         | 0.06    |
| D-Dimer^ (mg/dL) (n=129)                    | 4.9 (1.8 to 12.3) (n=114)                  | 1.9 (1.2 to 6.0) (n=15)                     | 0.04    |
| Ferritin^ (ng/mL) (n=129)                   | 1417 (671 to 2275) (n=116)                 | 1454 (809 to 1575) (n=13)                   | 0.50    |
| Lactate dehydrogenase^ (IU/L) (n=123)       | 596 (484 to 841) (n=116)                   | 629 (389 to 747) (n=7)                      | 0.81    |
### Tocilizumab for treatment of mechanically ventilated patients with COVID-19

| Laboratory Test | Value | p-value |
|-----------------|-------|---------|
| Aspartate aminotransferase<sup>+</sup> (IU/L) | 73 (47 to 123) (n=116) | 63 (51 to 107) (n=24) | 0.81 |
| Alanine aminotransferase<sup>+</sup> (IU/L) | 50 (30 to 80) (n=116) | 47 (30 to 75) (n=24) | 0.98 |
| Alkaline phosphatase<sup>+</sup> (IU/L) | 79.5 (60.0 to 113.0) (n=116) | 74.0 (56.0 to 99.0) (n=24) | 0.26 |
| Total bilirubin<sup>+</sup> (mg/dl) | 0.6 (0.4 to 1.0) (n=116) | 0.5 (0.4 to 0.9) (n=24) | 0.06 |

### Concomitant medications during hospitalization

| Medication | Outside Hospital | Michigan Medicine | p-value |
|------------|------------------|-------------------|---------|
| Tocilizumab | 49 (42) | 29 (76) | <0.001 |
| Hydroxychloroquine | 23 (20) | 12 (32) | 0.13 |
| Remdesivir | 2 (2) | 1 (3) | 0.73 |
| NSAIDs | 40 (34) | 13 (34) | 0.98 |
| Acetaminophen | 109 (94) | 37 (97) | 0.41 |
| ACE Inhibitors or Angiotensin Receptor Blockers | 13 (11) | 9 (24) | 0.06 |
| Vasopressors | 107 (92) | 33 (87) | 0.32 |
| Therapeutic anticoagulation | 85 (73) | 24 (63) | 0.23 |
| Corticosteroid usage | 25 (22) | 13 (34) | 0.12 |
| Methylprednisolone infusion | 15 (13) | 9 (24) | 0.11 |
| Oral prednisone | 10 (9) | 4 (11) | 0.72 |

### Timing of mechanical ventilation

| Time after presentation | Outside Hospital | Michigan Medicine | p-value |
|-------------------------|------------------|-------------------|---------|
| Within 24 hours of transfer | 18 (31) | 1 (7) | 0.09 |
| 24 – 48 hours prior to transfer | 18 (31) | 4 (27) | 0.09 |
| > 48 hours prior to transfer | 23 (39) | 10 (67) | 0.09 |
| In first 24 hours after presentation | 45 (79) | 7 (30) | <0.001 |
| 24 – 48 hours after presentation | 3 (5) | 4 (17) | <0.001 |
| > 48 hours after presentation | 9 (16) | 12 (52) | <0.001 |

### Timing of tocilizumab treatment

| Time after intubation | Outside Hospital | Michigan Medicine | p-value |
|-----------------------|------------------|-------------------|---------|
| Treated at Outside Hospital | 0 (0) | 3 (10) | <0.001 |
| Treated > 24 hours prior to intubation | 0 (0) | 6 (21) | <0.001 |
| Treated within 24 hours of intubation | 24 (49) | 13 (45) | <0.001 |
| Treated 24-48 hours after intubation | 11 (22) | 1 (3) | <0.001 |
| Treated > 48 hours after intubation | 14 (29) | 6 (21) | <0.001 |
Table S6. Hazard ratio estimates of the association between tocilizumab and survival.  
Time from intubation to death or censoring. Hazard ratio estimates for tocilizumab (treated vs. untreated) from each of the models below are displayed in Figure S3.

| Model                                | Hazard Ratio [95% CI] | p-value |
|--------------------------------------|-----------------------|---------|
| **Unadjusted**                        |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.50 [0.27, 0.90]     | 0.02    |
| **Stratum-specific sensitivity analyses** |                     |         |
| Male-only                             |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.53 [0.26, 1.06]     | 0.07    |
| Female-only                           |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.41 [0.13, 1.33]     | 0.14    |
| Age<70-only                           |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.55 [0.27, 1.13]     | 0.10    |
| Age<75-only                           |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.57 [0.29, 1.10]     | 0.09    |
| Age<60-only                           |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.59 [0.21, 1.72]     | 0.34    |
| Non-transfer-only                     |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.41 [0.15, 1.11]     | 0.08    |
| Transfer-only                         |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.54 [0.25, 1.13]     | 0.11    |
| CRP>150-only                          |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.48 [0.21, 1.11]     | 0.09    |
| D-Dimer>1.2-only                      |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.42 [0.19, 0.94]     | 0.03    |
| **Anticoag treated-only**             |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.58 [0.30, 1.14]     | 0.12    |
| **Anticoag untreated-only**           |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.24 [0.05, 1.08]     | 0.06    |
| **Bivariable models**                 |                       |         |
| Age-adjusted                          |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.55 [0.30, 1.01]     | 0.05    |
| Age (per 10 years)                    | 1.41 [1.13, 1.75]     | 0.002   |
| **Sex-adjusted**                      |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.49 [0.27, 0.89]     | 0.02    |
| Male vs. female                       | 1.39 [0.73, 2.64]     | 0.32    |
| **Race-adjusted**                     |                       |         |
| Tocilizumab: (treated vs. not-treated) | 0.49 [0.27, 0.89]     | 0.02    |
| Race: Black vs. white                 | 0.75 [0.37, 1.50]     | 0.41    |
| Race: Other vs. white                 | 1.16 [0.53, 2.55]     | 0.71    |
| Model                                           | Hazard Ratio [95% CI] | p-value |
|------------------------------------------------|------------------------|---------|
| Tocilizumab: (treated vs. not-treated)         | 0.52 [0.28, 0.94]      | 0.03    |
| Ethnicity: Hispanic vs. non-Hispanic           | ---*                  | ---*    |
| **BMI-adjusted**                               |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.50 [0.27, 0.91]      | 0.02    |
| BMI (per 5 kg/m²)                              | 0.92 [0.78, 1.08]      | 0.31    |
| **Hypertension-adjusted**                      |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.50 [0.27, 0.90]      | 0.02    |
| Hypertension (yes vs. no)                      | 1.23 [0.66, 2.31]      | 0.52    |
| **Congestive heart failure-adjusted**          |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.50 [0.28, 0.92]      | 0.03    |
| Congestive heart failure (yes vs. no)          | 2.16 [1.18, 3.93]      | 0.01    |
| **Chronic pulmonary disease-adjusted**         |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.53 [0.29, 0.98]      | 0.04    |
| Chronic pulmonary disease (yes vs. no)         | 1.47 [0.75, 2.89]      | 0.26    |
| **Asthma-adjusted**                            |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.49 [0.27, 0.90]      | 0.02    |
| Asthma (yes vs. no)                            | 1.60 [0.83, 3.09]      | 0.16    |
| **Sleep apnea-adjusted**                       |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.51 [0.28, 0.92]      | 0.03    |
| Sleep apnea (yes vs. no)                       | 1.32 [0.71, 2.45]      | 0.38    |
| **Diabetes-adjusted**                          |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.51 [0.28, 0.93]      | 0.03    |
| Diabetes (yes vs. no)                          | 1.50 [0.74, 3.04]      | 0.26    |
| **Renal disease-adjusted**                     |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.51 [0.28, 0.94]      | 0.03    |
| Renal disease (yes vs. no)                     | 1.32 [0.74, 2.37]      | 0.35    |
| **Transfer-adjusted**                          |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.49 [0.26, 0.89]      | 0.02    |
| Transfer patient (Yes vs. no)                  | 0.89 [0.48, 1.64]      | 0.70    |
| **Time to Vent-adjusted**                      |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.50 [0.27, 0.91]      | 0.02    |
| Days from admit to vent                        | 0.98 [0.84, 1.15]      | 0.82    |
| **HCQ-adjusted**                               |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.48 [0.26, 0.88]      | 0.02    |
| HCQ: (treated vs. not-treated)                 | 1.43 [0.75, 2.74]      | 0.27    |
| **Anticoag-adjusted**                          |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.52 [0.29, 0.93]      | 0.03    |
| Anticoag: (treated vs. not-treated)            | 2.58 [1.35, 4.96]      | 0.004   |
| **Methylprednisolone-adjusted**                |                        |         |
| Tocilizumab: (treated vs. not-treated)         | 0.49 [0.27, 0.89]      | 0.02    |
| Methylprednisolone: (treated vs. not)          | 1.36 [0.65, 2.81]      | 0.41    |
| Model | Hazard Ratio [95% CI] | p-value |
|-------|------------------------|---------|
| **Prone positioning-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.52 [0.28, 0.95] | 0.03 |
| Prone positioning: (yes vs. no) | 0.68 [0.31, 1.46] | 0.32 |
| **Temperature-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.39 [0.20, 0.76] | 0.01 |
| Temperature: (at admission per F) | 1.18 [1.00, 1.40] | 0.06 |
| **Albumin-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.46 [0.22, 0.95] | 0.04 |
| Albumin: (per g/dL) | 0.91 [0.47, 1.78] | 0.79 |
| **ALC-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.38 [0.18, 0.80] | 0.01 |
| ALC: (per 10⁹/L) | 0.61 [0.26, 1.39] | 0.24 |
| **AST-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.46 [0.24, 0.89] | 0.02 |
| AST: (per 10 g/dL) | 1.00 [1.00, 1.01] | 0.01 |
| **CRP-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.40 [0.20, 0.81] | 0.01 |
| CRP: (per 100 g/L) | 0.94 [0.76, 1.15] | 0.52 |
| **D-Dimer-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.36 [0.17, 0.78] | 0.01 |
| D-Dimer: (per 10 g/dL) | 1.09 [0.83, 1.42] | 0.53 |
| **Ferritin-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.48 [0.24, 0.98] | 0.04 |
| Ferritin: (per 1000 g/dL) | 1.14 [1.02, 1.27] | 0.02 |
| **LDH-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.37 [0.17, 0.80] | 0.01 |
| LDH: (per 100 U/L) | 1.09 [1.04, 1.14] | <0.001 |
| **WBC-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.41 [0.21, 0.82] | 0.01 |
| WBC: (per 10⁹/L) | 1.00 [0.95, 1.06] | 0.89 |
| **PaO2/FiO2-adjusted** | | |
| Tocilizumab: (treated vs. not-treated) | 0.35 [0.13, 0.97] | 0.04 |
| PaO2/FiO2: (per 10) | 0.98 [0.90, 1.07] | 0.62 |

### Multivariable models

#### Model A: Demographic adjusted

| Hazard Ratio [95% CI] | p-value |
|-----------------------|---------|
| Tocilizumab: (treated vs. not-treated) | 0.54 [0.29, 1.00] | 0.05 |
| Age (per 10 years) | 1.41 [1.13, 1.76] | 0.003 |
| Male vs. female | 1.47 [0.76, 2.82] | 0.25 |
| Race: Black vs. white | 0.97 [0.47, 1.99] | 0.94 |
| Race: Other vs. white | 1.48 [0.66, 3.29] | 0.34 |

Note: IPTW**b**
### Model

|                         | Hazard Ratio [95% CI] | p-value |
|-------------------------|-----------------------|---------|
| Tocilizumab: (treated vs. not-treated) | 0.55 [0.34, 0.90] | 0.02    |

#### Model B: Demographic + IPTW<sup>b</sup> adjusted

|                         | Hazard Ratio [95% CI] | p-value |
|-------------------------|-----------------------|---------|
| Tocilizumab: (treated vs. not-treated) | 0.55 [0.33, 0.90] | 0.02    |
| Age (per 10 years)      | 1.58 [1.32, 1.89]    | <0.001  |
| Male vs. female         | 2.36 [1.33, 4.20]    | 0.003   |
| Race: Black vs. white   | 1.09 [0.60, 1.97]    | 0.78    |
| Race: Other vs. white   | 1.75 [0.91, 3.33]    | 0.09    |

#### Model C: Demographic + IPTW-MI<sup>c</sup> adjusted

|                         | Hazard Ratio [95% CI] | p-value |
|-------------------------|-----------------------|---------|
| Tocilizumab: (treated vs. not-treated) | 0.54 [0.35, 0.84] | 0.01    |
| Age (per 10 years)      | 1.46 [1.25, 1.71]    | <0.001  |
| Male vs. female         | 1.75 [1.07, 2.85]    | 0.03    |
| Race: Black vs. white   | 1.16 [0.68, 1.98]    | 0.58    |
| Race: Other vs. white   | 1.65 [0.90, 3.03]    | 0.11    |

*There were no deaths out of the 3 Hispanics; hazard ratio estimates undefined.

<sup>a</sup> Demographic-adjusted=controlled for age, sex, and race as covariates

<sup>b</sup> IPTW=weighted by inverse probability of treatment group, based on the propensity score model shown in Table S3; the propensity score included the following variables: age, congestive heart failure, chronic pulmonary disease, chronic renal disease, therapeutic anticoagulation, ferritin, LDH, AST.

<sup>c</sup> MI=multiple imputation, used to impute missing laboratory values as relevant for ferritin, LDH, and/or AST. Twenty-five imputations by fully conditional specification were made based on age, sex, race, ethnicity, transfer status, history of hypertension, congestive heart failure, chronic pulmonary disease, and chronic renal disease.
Table S7. Odds ratio estimates of the association between of tocilizumab and clinical status (ordinal outcome) at Day 28.

Odds ratio (OR) estimates from proportional odds models represent OR per 1 level increase in the six-level ordinal outcome scale for illness severity including superinfections (see key for levels). Lower odds ratios are “favorable” (i.e., indicate decreased likelihood of worse outcomes). Odds ratio estimates for tocilizumab (treated vs. untreated) from each of the models below are displayed in Figure S4.

| Model                                      | Odds Ratio [95% CI] | p-value |
|--------------------------------------------|---------------------|---------|
| **Unadjusted**                             |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.57 [0.32, 1.01]   | 0.05    |
| **Stratum-specific sensitivity analyses**  |                     |         |
| Male-only                                  |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.56 [0.28, 1.13]   | 0.11    |
| Female-only                                |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.58 [0.22, 1.54]   | 0.27    |
| Age<70-only                                |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.62 [0.32, 1.18]   | 0.14    |
| Age<75-only                                |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.64 [0.35, 1.18]   | 0.15    |
| Age<60-only                                |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.80 [0.35, 1.80]   | 0.59    |
| Non-transfer-only                          |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.59 [0.21, 1.64]   | 0.31    |
| Transfer-only                              |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.59 [0.29, 1.18]   | 0.14    |
| CRP>150-only                               |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.54 [0.25, 1.14]   | 0.11    |
| D-Dimer>1.2-only                           |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.51 [0.25, 1.04]   | 0.06    |
| **Anticoag treated-only**                  |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.69 [0.35, 1.35]   | 0.28    |
| **Anticoag untreated-only**                |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.21 [0.06, 0.70]   | 0.01    |
| **Bivariable models**                      |                     |         |
| **Age-adjusted**                           |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.61 [0.34, 1.08]   | 0.09    |
| Age (per 10 years)                         | 1.18 [0.97, 1.43]   | 0.10    |
| **Sex-adjusted**                           |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.57 [0.32, 1.01]   | 0.05    |
| Male vs. female                            | 1.27 [0.70, 2.32]   | 0.43    |
| **Race-adjusted**                          |                     |         |
| Tocilizumab: (treated vs. not-treated)     | 0.56 [0.31, 0.99]   | 0.05    |
| Race: Black vs. white                      | 0.84 [0.57, 1.23]   | 0.37    |
| Race: Other vs. white                      | 1.18 [0.74, 1.89]   | 0.49    |

6-level ordinal outcome:
1. Discharged alive
2. Hospitalized, off vent, no superinfection
3. Hospitalized, off vent, with superinfection
4. Hospitalized, mechanically ventilated, no superinfection
5. Hospitalized, mechanically ventilated, with superinfection
6. Death
| Model                                         | Odds Ratio [95% CI] | p-value |
|-----------------------------------------------|---------------------|---------|
| Ethnicity-adjusted                            |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.58 [0.33, 1.03]   | 0.06    |
| Ethnicity: Hispanic vs. non-Hispanic          | 0.68 [0.08, 5.77]   | 0.73    |
| BMI-adjusted                                  |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.58 [0.32, 1.02]   | 0.06    |
| BMI (per 5 kg/m²)                             | 0.90 [0.77, 1.05]   | 0.17    |
| Hypertension-adjusted                         |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.57 [0.32, 1.01]   | 0.05    |
| Hypertension (yes vs. no)                     | 1.08 [0.59, 1.96]   | 0.81    |
| Congestive heart failure-adjusted             |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.58 [0.33, 1.02]   | 0.06    |
| Congestive heart failure (yes vs. no)         | 1.53 [0.78, 3.00]   | 0.21    |
| Chronic pulmonary disease-adjusted            |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.59 [0.33, 1.07]   | 0.08    |
| Chronic pulmonary disease (yes vs. no)        | 1.24 [0.59, 2.60]   | 0.57    |
| Asthma-adjusted                               |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.56 [0.32, 0.99]   | 0.05    |
| Asthma (yes vs. no)                           | 2.01 [0.99, 4.12]   | 0.05    |
| Sleep apnea-adjusted                          |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.57 [0.32, 1.01]   | 0.05    |
| Sleep apnea (yes vs. no)                      | 0.97 [0.51, 1.85]   | 0.93    |
| Diabetes-adjusted                             |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.57 [0.32, 1.02]   | 0.06    |
| Diabetes (yes vs. no)                         | 1.26 [0.58, 2.73]   | 0.55    |
| Renal disease-adjusted                        |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.60 [0.34, 1.07]   | 0.09    |
| Renal disease (yes vs. no)                    | 1.58 [0.88, 2.83]   | 0.12    |
| Transfer-adjusted                             |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.59 [0.33, 1.05]   | 0.07    |
| Transfer patient (Yes vs. no)                 | 1.21 [0.66, 2.21]   | 0.55    |
| Time to Vent-adjusted                         |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.56 [0.32, 1.00]   | 0.05    |
| Days from admit to vent                       | 1.02 [0.88, 1.17]   | 0.81    |
| HCQ-adjusted                                  |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.57 [0.32, 1.00]   | 0.05    |
| HCQ: (treated vs. not-treated)                | 1.06 [0.54, 2.08]   | 0.87    |
| Anticoag-adjusted                             |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.50 [0.28, 0.90]   | 0.02    |
| Anticoag: (treated vs. not-treated)           | 2.52 [1.32, 4.83]   | 0.01    |
| Methylprednisolone-adjusted                   |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.52 [0.29, 0.93]   | 0.03    |
| Methylprednisolone: (treated vs. not)         | 2.74 [1.23, 6.13]   | 0.01    |
| Prone positioning-adjusted                   |                     |         |
| Tocilizumab: (treated vs. not-treated)        | 0.55 [0.31, 0.98]   | 0.04    |
| Prone positioning: (yes vs. no)               | 1.28 [0.65, 2.53]   | 0.48    |
**Tocilizumab for treatment of mechanically ventilated patients with COVID-19**

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| Model               | Odds Ratio [95% CI] | p-value |
|---------------------|--------------------|---------|
| **Temperature-adjusted** |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.48 [0.26, 0.88] | 0.02    |
| Temperature: (at admission per F) | 1.14 [0.97, 1.36] | 0.12    |
| **Albumin-adjusted**      |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.59 [0.30, 1.14] | 0.11    |
| Albumin: (per g/dL) | 0.73 [0.37, 1.45] | 0.37    |
| **ALC-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.51 [0.26, 0.98] | 0.04    |
| ALC: (per 10⁹/L) | 0.62 [0.28, 1.37] | 0.24    |
| **ALT-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.53 [0.29, 0.97] | 0.04    |
| ALT: (per 10 g/dL) | 1.00 [0.99, 1.01] | 0.51    |
| **AST-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.53 [0.29, 0.98] | 0.04    |
| AST: (per 10 g/dL) | 1.01 [0.99, 1.02] | 0.36    |
| **CRP-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.57 [0.31, 1.06] | 0.08    |
| CRP: (per 100 g/L) | 1.00 [0.99, 1.01] | 0.98    |
| **D-Dimer-adjusted**     |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.53 [0.28, 1.01] | 0.05    |
| D-Dimer: (per 10 g/dL) | 1.18 [0.89, 1.57] | 0.26    |
| **Ferritin-adjusted**    |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.59 [0.31, 1.11] | 0.10    |
| Ferritin: (per 1000 g/dL) | 1.20 [1.03, 1.39] | 0.02    |
| **LDH-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.53 [0.28, 1.02] | 0.06    |
| LDH: (per 100 U/L) | 1.09 [1.00, 1.18] | 0.04    |
| **WBC-adjusted**         |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.51 [0.28, 0.94] | 0.03    |
| WBC: (per 10⁹/L) | 1.01 [0.96, 1.06] | 0.75    |
| **PaO2/FiO2-adjusted**   |                    |         |
| Tocilizumab: (treated vs. not-treated) | 0.38 [0.15, 0.94] | 0.04    |
| PaO2/FiO2: (per 10) | 0.94 [0.87, 1.02] | 0.11    |
| **Multivariable models** |                    |         |
| **Model A: Demographic adjusted** |            |         |
| Tocilizumab: (treated vs. not-treated) | 0.60 [0.34, 1.08] | 0.09    |
| Age (per 10 years) | 1.18 [0.97, 1.44] | 0.11    |
| Male vs. female | 1.29 [0.70, 2.36] | 0.41    |
| Race: Black vs. white | 0.89 [0.60, 1.31] | 0.56    |
| Race: Other vs. white | 1.22 [0.76, 1.95] | 0.42    |
| **Model B: Demographic + IPTW adjusted** |         |         |
| Tocilizumab: (treated vs. not-treated) | 0.56 [0.35, 0.89] | 0.02    |
| Age (per 10 years) | 1.27 [1.08, 1.49] | 0.004   |
| Model | Odds Ratio [95% CI] | p-value |
|-------|---------------------|---------|
| Male vs. female | 2.00 [1.20, 3.33] | 0.01 |
| Race: Black vs. white | 0.83 [0.60, 1.14] | 0.25 |
| Race: Other vs. white | 1.53 [1.04, 2.26] | 0.03 |
| **Model C: Demographic + IPTW-MI^c adj.** | | |
| Tocilizumab: (treated vs. not-treated) | 0.60 [0.39, 0.91] | 0.02 |
| Age (per 10 years) | 1.24 [1.08, 1.43] | 0.003 |
| Male vs. female | 1.67 [1.08, 2.58] | 0.02 |
| Race: Black vs. white | 0.90 [0.68, 1.20] | 0.48 |
| Race: Other vs. white | 1.20 [0.85, 1.68] | 0.30 |

^ Demographic-adjusted=controlled for age, sex, and race as covariates  
^ IPTW=weighted by inverse probability of treatment group, ba used on the propensity score model shown in Table S3; the propensity score included the following variables: age, congestive heart failure, chronic pulmonary disease, chronic renal disease, therapeutic anticoagulation, ferritin, LDH, AST.  
^ MI=multiple imputation, used to impute missing laboratory values as relevant for ferritin, LDH, and/or AST. Twenty-five imputations by fully conditional specification were made based on age, sex, race, ethnicity, transfer status, history of hypertension, congestive heart failure, chronic pulmonary disease, and chronic renal disease.