

# Supplementary Materials: Safety of Tocilizumab in COVID-19 Patients and Benefit of Single-Dose: The Largest Retrospective Observational Study

Ayman M. Al-Qaaneh, Fuad H. Al-Ghamdi, Sayed AbdulAzeez and J. Francis Borgio

**Table S1.** Clinical effectiveness of tocilizumab in treating patients with COVID-19 in different countries.

| Study reference | Date           | Country                    | n   | Outcome  |           |                                      |
|-----------------|----------------|----------------------------|-----|--|-----------|--------------------------------------|
|                 |                |                            |     | Favor  | Not favor | No difference                        |
| 33605118 [1]    | January 2021   | Saudi Arabia               | 40  | X  |           |                                      |
| 34479079 [2]    | September 2021 | Saudi Arabia               | 37  |  | X         |                                      |
| 33085857 [3]    | December 2020  | USA                        | 161 |  |           | X                                    |
| 34153727 [4]    | May 2021       | Saudi Arabia               | 62  | X  |           |                                      |
| 33472855 [5]    | January 2021   | Brazil                     | 65  |  | X         |                                      |
| 33080005[6]     | January 2021   | Italy                      | 60  |  |           | X                                    |
| 32405160 [7]    | May 2020       | Italy                      | 62  | X  |           |                                      |
| PMC7548660[8]   | October 2020   | USA                        | 44  | X  |           |                                      |
| MedRxiv [9]     | April 2020     | France                     | 30  | X  |           |                                      |
| MedRxiv [10]    | May 2020       | USA                        | 21  | X  |           |                                      |
| 32448770 [11]   | June 2020      | Italy                      | 51  |  |           | X                                    |
| 32570043 [12]   | May 2020       | Italy                      | 42  |  | X         |                                      |
| 32838323 [13]   | August 2020    | USA                        | 210 | X  |           |                                      |
| 32691021 [14]   | July 2020      | India                      | 70  | X  |           |                                      |
| 32835257 [15]   | June 2020      | Italy                      | 179 | X  |           |                                      |
| 33169088 [16]   | December 2020  | Saudi Arabia               | 61  |  |           | X                                    |
| MedRxiv [17]    | June 2020      | Spain                      | 77  | X  |           |                                      |
| 32397399 [18]   | May 2020       | Italy                      | 21  |  |           | X                                    |
| 32387320 [19]   | August 2020    | France                     | 20  | X  |           |                                      |
| 33631065 [20]   | February 2021  | Multinational <sup>a</sup> | 353 | X  |           |                                      |
| 33631066 [21]   | April 2021     | Multinational <sup>b</sup> | 294 |  |           | X                                    |
| 33332779 [22]   | December 2020  | Multinational <sup>c</sup> | 249 | X (time to mechanical ventilation or death)                                |           | Survival                             |
| 32744399 [23]   | August 2021    | Sweden                     | 29  | X (time on mechanical ventilation and length of hospital stay)             |           | Mortality                            |
| 33605108 [24]   | June 2021      | Oman                       | 62  | X (ventilator parameter and extubation)                                    |           | mortality                            |
| 33080017 [25]   | January 2021   | France                     | 64  | X (noninvasive ventilation, mechanical ventilation, and 14 days mortality) |           | WHO-CPS scores and 28 days mortality |

<sup>a</sup> United Kingdom, Netherlands, Australia, New Zealand, Ireland, Saudi Arabia ( $n = 83$ ); <sup>b</sup> Canada, Denmark, France, Italy, Germany, Netherlands, Spain, United Kingdom, and the USA; <sup>c</sup> United States, Peru, Brazil, Kenya, South Africa, Mexico.

**Table S2.** Extracted data from the electronic health record system (EPIC®) for COVID-19 patients on tocilizumab.

| Parameters   |  |
|--|--|
| Demographical data   |  |
| Patient age  |  |
| Gender   | Male   |
|  | Female   |
| Nationality  | Saudi  |
|  | Non-Saudi  |
| Patient weight (kg)  |  |
| Body mass index (BMI) (Normal: 18.5–24.9 kg/m <sup>2</sup> ) |  |
| Smoking status   |  |
| Smoking status   | Non-smoker   |
|  | Former-smoker  |
|  | Active-smoker  |
| Clinical characteristics                                     |  |
| Comorbid Conditions  | Hypertension   |
|  | Cardiac diseases include pericardiac effusion, coronary artery diseases, diastolic dysfunction, congestive heart failure, cardiomyopathy, and other cardiovascular diseases) |
|  | Dyslipidemia   |
|  | Diabetes Mellitus include diabetes mellitus type I & II  |
|  | Respiratory diseases include asthma, pneumonia, acute respiratory failure, chronic obstructive pulmonary disease, pleural effusion, and other lung diseases.                 |
|  | Thyroid diseases include hyperthyroidism, hypothyroidism, and other thyroid diseases.  |
|  | Kidney diseases include chronic kidney disease and acute kidney disease.   |
|  | Arthritis includes arthritis and rheumatoid arthritis  |
|  | Sickle cell disease  |
|  | Stroke   |
|  | Cancer   |
|  | Gastrointestinal diseases  |
|  | Osteopenia/osteoporosis  |
|  | Gout   |
|  | Peripheral vascular diseases include peripheral vascular disease and varicose veins.   |
|  | Anemia   |
|  | Deep venous thrombosis   |
|  | Glucose 6 Phosphate Dehydrogenase Deficiency (G6PD)  |
|  | Liver diseases include hepatitis (A, B, and C), fatty liver, and liver cirrhosis   |
|  | Autoimmune diseases and Immunosuppressed patients  |
| Concurrent drugs administration                              |  |
| Antiviral drug   | Lopinavir/Ritonavir  |
|  | Favipiravir  |
|  | Oseltamivir  |
| Corticosteroids  | Dexamethasone  |
|  | Methylprednisolone   |
|  | Hydrocortisone   |
|  | Prednisone/prednisolone  |
| Hydroxychloroquine   |  |
| Hospital related parameters                                  |  |
| Hospital admission date                                      |  |
| Hospital discharge date                                      |  |
| Date of death  |  |
| ICU related parameters                                       |  |
| ICU admission (Yes/No)                                       |  |
| ICU admission date   |  |
| ICU discharge date   |  |

|   |  |                     |
|---|--|---------------------|
| Tocilizumab related parameters  |  |                     |
| Number of tocilizumab doses   |  |                     |
| Amount of tocilizumab dose (mg)   |  |                     |
| Time and date of the tocilizumab dose   |  |                     |
| The location where the tocilizumab dose was administered; ICU or Non-ICU            |  |                     |
| Laboratory related parameters   |  |                     |
| All included laboratory results at the time of admission till the time of discharge |  |                     |
| Laboratory results  |  |                     |
| Test group  | Individual test                                  | Normal range        |
| Electrolyte   | Sodium   | 135–145 mEq/L       |
|   | Potassium  | 3.5–5.1 mEq/L       |
|   | Calcium  | 8.6–10.0 mg/dL      |
|   | Magnesium  | 1.7–2.4 mg/dL       |
|   | Phosphorus                                       | 2.5–4.5 mg/dL       |
|   | Chloride   | 98–107 mEq/L        |
|   | Carbon Dioxide                                   | 22–28 mEq/L         |
| Chemical profile  | Blood Urea Nitrogen (BUN)                        | 6–20 mg/dL          |
|   | Creatinine                                       | 0.66–1.25 mg/dL     |
|   | Blood Glucose Level                              | 73–178 mg/dL        |
| Cardiac profile   | Troponin High Sensitive                          | 0.000–0.026 ng/mL   |
|   | B-type Natriuretic Peptide                       | <100 pg/mL          |
| Hepatic profile   | Bilirubin, Total                                 | 0.2–1.3 mg/dL       |
|   | Alkaline Phosphatase (ALP)                       | 53–128 IU/L         |
|   | Alanine Aminotransferase (ALT) (SGPT)            | <50 IU/L            |
|   | Aspartate Aminotransferase (AST) (SGOT)          | 17–59 IU/L          |
|   | Lactate Dehydrogenase (LDH)                      | 120–246 IU/L        |
| Iron/Anemia Profile   | Ferritin   | 21.81–274.66 ng/mL  |
| C-Reactive protein (CRP)  | CRP  | <1.0 mg/dL          |
| Complete blood count  | White Blood Cell (WBC) count                     | 4.0–10.0 K/ $\mu$ L |
|   | Red Blood Corpuscles (RBC) count                 | 4.5–5.9 M/ $\mu$ L  |
|   | Hemoglobin concentration                         | 13.5–17.5 g/dL      |
|   | Hematocrit                                       | 41–53 %             |
|   | Mean Corpuscular Volume (MCV)                    | 77–96 fL            |
|   | Mean Corpuscular Hemoglobin (MCH)                | 26–34 pg            |
|   | Mean Corpuscular Hemoglobin Concentration (MCHC) | 32–36 g/dL          |
|   | Red Corpuscular Distribution Width (RDW)         | 10.9–15.7           |
|   | Platelets  | 150–450 K/ $\mu$ L  |
|   | Mean Platelet Volume                             | 9.0–13.0 fL         |
|   | Platelets Distribution Width                     | 10.1–16.1 fL        |
|   | Neutrophils Absolute                             | 1.8–7.0 K/ $\mu$ L  |
|   | Lymphocytes Absolute                             | 0.9–4.9 K/ $\mu$ L  |
|   | Monocytes Absolute                               | 0.0–1.0 K/ $\mu$ L  |
|   | Eosinophils Absolute                             | 0.0–0.4 K/ $\mu$ L  |
|   | Basophils Absolute                               | 0.0–0.1 K/ $\mu$ L  |
|   | Band Neutrophil Absolute                         | 0.0–0.5 K/ $\mu$ L  |
| Coagulation   | Prothrombin Time                                 | 9.8–12.7 Secs       |
|   | International Normalization Ratio (INR)          | 1.0–1.2 Ratio       |
|   | Activated Partial Thromboplastin Time (APTT)     | 22–33 Secs          |
| Urine analysis  | D-Dimer Quantitative                             | 0.0–0.7 mg/L FEU    |
|   | Urine Specific Gravity                           | 1.000–1.030         |
|   | Urine pH   | 4.5–8.0             |
|   | Urine Protein                                    | Negative            |
|   | Urine Glucose                                    | Negative            |
|   | Urine Ketone                                     | Negative            |
|   | Urine Blood                                      | Negative            |
|   | Urine Bilirubin                                  | Negative            |

|                          |               |
|--------------------------|---------------|
| Urine Urobilinogen       | 0.0–1.0 EU/dL |
| Urine Nitrites           | Negative      |
| Urine Leukocyte Esterase | Negative      |

**Table S3.** List of calculated parameters.

| Parameters  |
|---|
| Demographical Calculated parameters   |
| <p>➤ <b>Body mass index groups:</b><br/>Body mass index values are collapsed and grouped into one of the main BMI groups based on the Centers for Disease Control and Prevention (CDC) classification [26] as below:</p> <ul style="list-style-type: none"> <li>○ Underweight &lt;18.5 kg/m<sup>2</sup></li> <li>○ Normal weight 18.5–24.9 kg/m<sup>2</sup></li> <li>○ Overweight 25.0–29.9 kg/m<sup>2</sup></li> <li>○ Obese &gt;30.0 kg/m<sup>2</sup></li> </ul>  |
| Clinical calculated parameters  |
| <p>➤ <b>Number of comorbidities:</b><br/>Patients are classified into four groups based on the number of comorbidities they had before hospital admission:</p> <ul style="list-style-type: none"> <li>○ Patients have no comorbidity</li> <li>○ Patients have one comorbidity</li> <li>○ Patients have two comorbidities</li> <li>○ Patients have three and more comorbidities</li> </ul>   |
| Concurrent drugs calculated parameters  |
| <p>Patients are classified into three groups based on <b>co-administered medications during their COVID-19 admission</b></p> <ul style="list-style-type: none"> <li>○ Patients received at least one type of antiviral drugs</li> <li>○ Patients received at least one type of corticosteroids</li> <li>○ Patients received Hydroxychloroquine</li> </ul>   |
| Hospital and ICU calculated parameters  |
| <p>➤ <b>Days to ICU admission</b> for patients admitted to ICU: ICU admission date – Hospital admission date</p> <p>➤ <b>Days to death</b> for deceased patients: Death date – Hospital admission date</p> <p>➤ <b>Total ICU length of stay</b> for patients admitted to ICU: ICU discharge date–ICU admission date</p> <p>➤ <b>Hospital length of stay:</b> Hospital discharge date – Hospital admission date</p>  |
| Tocilizumab calculated parameters   |
| <p>➤ <b>Days to the first dose of tocilizumab:</b> Date of the first dose of tocilizumab – Hospital admission date</p> <p>➤ <b>Days from ICU admission to the first dose of tocilizumab</b> for patients admitted to ICU: Date of the first dose of tocilizumab – ICU admission date</p> <p>➤ <b>Hospital length of stay after the nth dose of tocilizumab:</b> Hospital discharge date – Date of nth dose of tocilizumab</p> <p>➤ <b>ICU length of stay after the nth dose of tocilizumab</b> for patients received the nth dose of tocilizumab in ICU or admitted to ICU after the nth dose of tocilizumab:</p> <ul style="list-style-type: none"> <li>○ ICU discharge date – date of the nth dose of tocilizumab; for patients who received the nth dose of tocilizumab in ICU</li> <li>○ ICU discharge date – ICU admission date for; patients admitted to ICU after the nth dose of tocilizumab</li> </ul> <p>➤ <b>Days to death after the nth dose of tocilizumab:</b> Date of death – date of the nth dose of tocilizumab</p> <p>➤ <b>Days to the next dose of tocilizumab:</b> date of the n<sup>th</sup>+1 dose of tocilizumab – date of the nth dose of tocilizumab</p> <p>➤ <b>Days between the first and third dose of tocilizumab</b> for patients received three doses of tocilizumab: Date of the third dose of tocilizumab – date of the first dose of tocilizumab</p> <p>➤ <b>Total mg of tocilizumab:</b> summation of all milligrams of tocilizumab administered by the patient during his/her COVID-19 admission</p> <p>➤ <b>Total mg of tocilizumab in groups</b><br/>Patients are classified into four groups based on the total mg of tocilizumab administered:</p> <ul style="list-style-type: none"> <li>○ Patients received a total dose of tocilizumab &lt; 800 mg</li> <li>○ Patients received a total dose of tocilizumab 801–1600 mg</li> <li>○ Patients received a total dose of tocilizumab 1601–2400 mg</li> <li>○ Patients received a total dose of tocilizumab &gt;2400 mg</li> </ul> <p>➤ <b>Total mg/kg of tocilizumab</b> received by the penitent: Total mg of tocilizumab received by the patient divided by the patient actual body weight</p> <p>➤ <b>Total mg/kg of tocilizumab in groups</b><br/>Patients are classified into four groups based on the total mg/kg of tocilizumab administered:</p> <ul style="list-style-type: none"> <li>○ Patients received a total dose of tocilizumab &lt;10 mg/kg</li> <li>○ Patients received a total dose of tocilizumab 10.1–21 mg/kg</li> <li>○ Patients received a total dose of tocilizumab 21.1–32 mg/kg</li> <li>○ Patients received a total dose of tocilizumab &gt; 32 mg/kg</li> </ul> |
| Laboratory calculated parameters  |
| <p>➤ Patients are classified into two groups based on their <b>urine protein, urine glucose, urine ketone, urine bilirubin, urine urobilinogen, urine nitrites, and urine leukocyte esterase:</b> negative or available.</p>  |

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➤ Patients are classified into four groups based on the **amount of blood in their urine sample**: negative, trace, moderate, or numerous.

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**Table S4.** Clinical & laboratory parameters and outcome measures of COVID-19 patients on tocilizumab (survived= 237 & diseased= 63).

| Parameters   |  | Total Patients' Count<br>(%), Mean (SD), or Median (IQR) | Survivors' Count (%),<br>Mean (SD), or Median (IQR) | Non-survivors' Count<br>(%), Mean (SD), or Median (IQR) | <i>p</i> -value               |
|--|--|--|---|---|-------------------------------|
| Number of patients ( <i>n</i> , %)                                     |  | 300 (100%)   | 237 (79%)   | 63 (21%)  | 0.020932 *i                   |
| Mortality for ICU patients   |  |  |   |   |                               |
| Number of patients admitted to ICU ( <i>n</i> , %)                     |  | 161 (100%)   | 99 (61.5%)  | 62 (38.5%)  | 0.042259 *ii                  |
| Demographical Characteristics  |  |  |   |   |                               |
| Age (year) median (IQR)  |  | 63 (55.00–71.00)   | 60.00 (53.50–68.00)                                 | 70.00 (64.00–79.00)                                     | 1.3416 × 10 <sup>-8</sup> *** |
| Gender   | Male ( <i>n</i> , %)                                 | 196 (65.3%)  | 157 (66.2%)   | 39 (61.9%)  | 0.552735                      |
|  | Female ( <i>n</i> , %)                               | 104 (34.7%)  | 80 (33.8%)  | 24 (38.1%)  |                               |
| Nationality  | Saudi ( <i>n</i> , %)                                | 281 (93.7%)  | 220 (93.2%)   | 61 (96.8%)  | 0.381512                      |
|  | Non-Saudi ( <i>n</i> , %)                            | 18 (6.0%)  | 16 (6.8%)   | 2 (3.2%)  |                               |
| Weight (kg) median (IQR)   |  | 83.00 (72.23–95.75)                                      | 83.00 (73.10–96.00)                                 | 82.70 (70.70–94.50)                                     | 0.598736                      |
| Body mass index (kg/m <sup>2</sup> ) median (IQR))                     |  | 31.36 (27.43–35.76)                                      | 31.26 (27.52–35.63)                                 | 31.63 (27.33–36.33)                                     | 0.968066                      |
| Body Mass Index category   | Underweight (<18.5) ( <i>n</i> , %)                  | 3 (1.0%)   | 3 (1.3%)  | 0 (0.0%)  | 0.060835                      |
|  | Normal weight (18.5–24.9) ( <i>n</i> , %)            | 27 (9.0%)  | 16 (6.8%)   | 11 (17.5%)  |                               |
|  | Overweight (25.0–29.9) ( <i>n</i> , %)               | 94 (31.3%)   | 78 (32.9%)  | 16 (25.4%)  |                               |
|  | Obese (>35.0) ( <i>n</i> , %)                        | 176 (58.7%)  | 140 (59.1%)   | 36 (57.1%)  |                               |
| Smoking status   | Non-smoker ( <i>n</i> , %)                           | 235 (78.3%)  | 183 (77.2%)   | 52 (82.5%)  | 0.402420                      |
|  | Former-smoker ( <i>n</i> , %)                        | 39 (13.0%)   | 34 (14.3%)  | 5 (7.9%)  |                               |
|  | Active-smoker ( <i>n</i> , %)                        | 26 (8.8%)  | 20 (8.6%)   | 6 (9.5%)  |                               |
| Clinical Characteristics   |  |  |   |   |                               |
| Number of Comorbidities  | 0 ( <i>n</i> , %)                                    | 73 (24.3%)   | 64 (27%)  | 9 (14.3%)   | 0.000083 ***                  |
|  | 1 ( <i>n</i> , %)                                    | 68 (22.7%)   | 57 (24.1%)  | 11 (17.5%)  |                               |
|  | 2 ( <i>n</i> , %)                                    | 60 (20.0%)   | 53 (22.4%)  | 7 (11.1%)   |                               |
|  | 3 or more ( <i>n</i> , %)                            | 99 (33.0%)   | 63 (26.6%)  | 36 (57.1%)  |                               |
| Comorbid Conditions  | Hypertension ( <i>n</i> , %)                         | 94 (31.3%)   | 63 (26.6%)  | 31 (49.2%)  | 0.001176 **                   |
|  | Cardiac diseases ( <i>n</i> , %)                     | 47 (15.7%)   | 23 (9.7%)   | 24 (38.1%)  | 4.3734 × 10 <sup>-7</sup> *** |
|  | Dyslipidemia ( <i>n</i> , %)                         | 63 (21.0%)   | 44 (18.6%)  | 19 (30.2%)  | 0.055286                      |
|  | Diabetes mellitus ( <i>n</i> , %)                    | 153 (51.0%)  | 113 (47.7%)   | 40 (63.5%)  | 0.033037 *                    |
|  | Respiratory diseases ( <i>n</i> , %)                 | 23 (7.7%)  | 17 (7.2%)   | 9 (9.5%)  | 0.593632                      |
|  | Thyroid diseases ( <i>n</i> , %)                     | 21 (7.0%)  | 16 (6.8%)   | 5 (7.9%)  | 0.781515                      |
|  | Kidney diseases ( <i>n</i> , %)                      | 21 (7.0%)  | 13 (5.5%)   | 8 (12.7%)   | 0.054929                      |
|  | Arthritis ( <i>n</i> , %)                            | 32 (10.7%)   | 20 (8.4%)   | 12 (19%)  | 0.021439 *                    |
|  | Sickle cell disease ( <i>n</i> , %)                  | 15 (5.0%)  | 11 (4.6%)   | 4 (6.3%)  | 0.527662                      |
|  | Stroke ( <i>n</i> , %)                               | 7 (2.3%)   | 5 (2.1%)  | 2 (3.2%)  | 0.640250                      |
|  | Cancer ( <i>n</i> , %)                               | 23 (7.7%)  | 13 (5.5%)   | 10 (15.9%)  | 0.013156 *                    |
|  | Gastrointestinal diseases ( <i>n</i> , %)            | 21 (7.0%)  | 19 (8.0%)   | 2 (3.2%)  | 0.267006                      |
|  | Osteopenia/Osteoporosis ( <i>n</i> , %)              | 12 (4.0%)  | 6 (2.5%)  | 6 (9.5%)  | 0.022015 *                    |
|  | Gout ( <i>n</i> , %)                                 | 2 (0.7%)   | 2 (0.8%)  | 0 (0.0%)  | 1.000000                      |
|  | Peripheral vascular disease ( <i>n</i> , %)          | 3 (1.0%)   | 3 (1.3%)  | 0 (0.0%)  | 1.000000                      |
|  | Anemia ( <i>n</i> , %)                               | 17 (5.7%)  | 10 (4.2%)   | 7 (5.7%)  | 0.058971                      |
|  | Deep venous thrombosis ( <i>n</i> , %)               | 4 (1.3%)   | 2 (0.8%)  | 2 (3.2%)  | 0.195364                      |
|  | G6PD deficiency ( <i>n</i> , %)                      | 43 (14.3%)   | 34 (14.3%)  | 9 (14.3%)   | 1.000000                      |
|  | Liver diseases ( <i>n</i> , %)                       | 6 (2.0%)   | 3 (1.3%)  | 3 (4.8%)  | 0.109455                      |
|  | Autoimmune diseases/Immunosuppressed ( <i>n</i> , %) | 2 (0.7%)   | 2 (0.8%)  | 0 (0.0%)  | 1.000000                      |
| Concurrent Drug Administration   |  |  |   |   |                               |
| Patients received at least one type of antiviral drugs ( <i>n</i> , %) |  | 64 (21.3%)   | 40 (16.9%)  | 24 (38.1%)  | 0.000258 ***                  |
| Patient received at least one type of corticosteroids ( <i>n</i> , %)  |  | 298 (99.3)   | 235 (99.2%)   | 63 (100.0%)   | 1.000000                      |
| Patient received hydroxychloroquine ( <i>n</i> , %)                    |  | 63 (21%)   | 45 (19.0%)  | 18 (28.6%)  | 0.096912                      |
| Laboratory Characteristics   |  |  |   |   |                               |
| Electrolytes   |  |  |   |   |                               |
| Sodium (135–145 mEq/L) median (IQR)                                    |  | 136.00 (133.00–138.00)                                   | 136.00 (134.00–138.00)                              | 135.62 (132.00–139.00)                                  | 0.528234                      |
| Potassium (3.5–5.1 mEq/L) median (IQR)                                 |  | 4.30 (4.10–4.70)   | 4.30 (4.00–4.70)                                    | 4.40 (4.10–4.80)  | 0.075398                      |
| Calcium (8.6–10.0 mg/dL ) median (IQR)                                 |  | 8.40 (8.10–8.80)   | 8.40 (8.10–8.78)                                    | 8.40 (8.10–8.80)  | 0.875897                      |
| Magnesium (1.7–2.4 mg/dL) median (IQR)                                 |  | 2.00 (1.80–2.30)   | 2.00 (1.80–2.20)                                    | 2.00 (1.90–2.30)  | 0.354069                      |
| Phosphorus (2.5–4.5 mg/dL) median (IQR)                                |  | 3.50 (3.00–4.10)   | 3.40 (3.00–3.80)                                    | 3.90 (3.20–5.03)  | 0.027015*                     |

|   |                         |                         |                          |                               |
|---|-------------------------|-------------------------|--------------------------|-------------------------------|
| Chloride (98–107 mEq/L) median (IQR)                      | 101.00 (98.00–103.00)   | 101.00 (98.00–103.00)   | 100.00 (96.00–104.00)    | 0.367070                      |
| Carbon Dioxide (22–28 mEq/L) median (IQR)                 | 25.00 (22.00–27.00)     | 25.00 (23.00–27.00)     | 24.00 (22.00–28.00)      | 0.827208                      |
| Chemical Profile  |                         |                         |                          |                               |
| Blood Urea Nitrogen (6–20 mg/dL) median (IQR)             | 19.00 (14.00–27.00)     | 17.00 (13.00–24.00)     | 26.00 (18.00–45.00)      | 2.3372 × 10 <sup>-7</sup> *** |
| Creatinine (0.66–1.25 mg/dL) median (IQR)                 | 0.80 (0.60–1.10)        | 0.80 (0.60–1.00)        | 1.00 (0.70–1.70)         | 0.000085 ***                  |
| Blood Glucose Level (73–178 mg/dL) median (IQR)           | 141.50 (111.75–210.50)  | 139.00 (110.00–211.00)  | 149.00 (114.00–205.00)   | 0.663107                      |
| Lactic Acid (0.7–2.1 mmol/L) median (IQR)                 | 1.50 (1.10–2.00)        | 1.50 (1.10–1.93)        | 1.45 (1.10–2.00)         | 0.930610                      |
| Cardiac Profile   |                         |                         |                          |                               |
| Troponin High Sensitive (0.000–0.026 ng/mL ) median (IQR) | 0.0100 (0.0045–0.0285)  | 0.0080 (0.0040–0.0195)  | 0.0190 (0.0095–0.0750)   | 0.000656 ***                  |
| B-type Natriuretic Peptide (<100 pg/mL) median (IQR)      | 59.00 (20.20–127.20)    | 44.30 (17.40–107.30)    | 96.05 (39.70–229.38)     | 0.009786 **                   |
| Hepatic Profile   |                         |                         |                          |                               |
| Bilirubin, Total (0.2–1.3 mg/dL) median (IQR)             | 0.5000 (0.4000–0.7000)  | 0.5000 (0.4000–0.7000)  | 0.5000 (0.4000–0.8000)   | 0.568120                      |
| Alk. Phosphatase (53 – 128 IU/L) median (IQR)             | 68.00 (56.00–87.00)     | 68.00 (55.00–85.00)     | 70.00 (58.00–97.00)      | 0.236349                      |
| ALT (SGPT) (<50 IU/L) median (IQR)                        | 31.00 (21.00–48.00)     | 31.00 (21.00–49.00)     | 29.00 (22.00–39.00)      | 0.539727                      |
| AST (SGOT) (17–59 IU/L) median (IQR)                      | 44.50 (35.00–62.50)     | 44.00 (34.00–62.00)     | 46.00 (37.00–77.00)      | 0.157338                      |
| LDH (120–246 IU/L) median (IQR)                           | 356.50 (280.00–462.00)  | 344.00 (275.00–450.50)  | 403.00 (337.00–558.00)   | 0.005640 **                   |
| Iron/Anemia Profile                                       |                         |                         |                          |                               |
| Ferritin (21.81–274.66 ng/mL) median (IQR)                | 786.00 (421.00–1538.00) | 672.00 (355.00–1283.00) | 1205.50 (586.25–2141.50) | 0.003288 **                   |
| CRP, Quantitative   |                         |                         |                          |                               |
| CRP, Quantitative (<1.0 mg/dL) median (IQR)               | 15.60 (6.30–20.40)      | 16.00 (6.18–20.85)      | 15.15 (6.53–19.65)       | 0.701715                      |
| Complete Blood Count                                      |                         |                         |                          |                               |
| WBC (4.0–10.0 K/μL) median (IQR)                          | 7.45 (5.30–10.10)       | 7.50 (5.25–10.10)       | 7.00 (5.30–10.40)        | 0.834314                      |
| RBC (4.5–5.9 M/μL) median (IQR)                           | 4.61 (4.15–5.11)        | 4.66 (4.22–5.16)        | 4.42 (3.83–4.76)         | 0.003536 **                   |
| Hemoglobin (13.5–17.5 g/dL) (mean ± SD)                   | 12.31 ±1.89             | 12.40±1.87              | 11.97±1.93               | 0.106621                      |
| Hematocrit (41–53 %) (mean ± SD)                          | 38.05 ±5.34             | 38.34±5.16              | 36.99±5.89               | 0.075295                      |
| MCV (77–96 fL) median (IQR)                               | 84.00 (77.30–88.38)     | 83.40 (77.25–87.75)     | 87.00 (77.30–90.10)      | 0.011527 *                    |
| MCH (26–34 pg) median (IQR)                               | 27.30 (24.80–29.18)     | 27.00 (24.60–29.10)     | 27.90 (25.90–29.60)      | 0.064683                      |
| MCHC (32–36 g/dL) median (IQR)                            | 32.40 (31.30–33.40)     | 32.50 (31.30–33.40)     | 32.30 (31.20–33.30)      | 0.779223                      |
| RDW (10.9–15.7) median (IQR)                              | 13.75 (12.90–14.80)     | 13.60 (12.80–14.65)     | 14.30 (13.00–15.70)      | 0.008499 **                   |
| Platelets (150–450 K/μL) median (IQR)                     | 233.00 (183.00–297.75)  | 240.00 (188.50–302.50)  | 209.00 (155.00–259.00)   | 0.007864 **                   |
| Mean Platelet Volume (9.0–13.0 fL) median (IQR)           | 10.60 (10.00–11.30)     | 10.60 (9.90–11.30)      | 10.60 (10.00–11.45)      | 0.436157                      |
| Platelets Distribution Width (10.1–16.1 fL) median (IQR)  | 12.30 (11.20–14.10)     | 12.30 (11.15–14.00)     | 12.70 (11.35–15.20)      | 0.156941                      |
| Neut. Absolute (1.8–7.0 K/μL) median (IQR)                | 6.05 (3.80–8.50)        | 6.10 (3.80–8.25)        | 5.40 (4.00–8.60)         | 0.771765                      |
| Lymph. Absolute (0.9–4.9 K/μL) median (IQR)               | 0.8000 (0.6000–1.1000)  | 0.8000 (0.6000–1.1000)  | .7000 (0.4000–0.9000)    | 0.022830 *                    |
| Mono. Absolute (0.0–1.0 K/μL) median (IQR)                | 0.3000 (0.2000–0.5000)  | 0.3000 (0.2000–0.5000)  | 0.3000 (0.2000–0.6000)   | 0.635995                      |
| Eos. Absolute (0.0–0.4 K/μL) median (IQR)                 | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000)   | 0.144171                      |
| Baso. Absolute (0.0–0.1 K/μL) median (IQR)                | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000)   | 0.144171                      |
| Band Neutrophil Absolute (0.0–0.5 K/μL) median (IQR)      | 0.2700 (0.1300–0.5900)  | .2600 (0.1300–0.6150)   | .3200 (0.1300–0.5400)    | 0.801130                      |
| Coagulation   |                         |                         |                          |                               |
| Prothrombin Time (9.8–12.7 Secs) median (IQR)             | 11.30 (10.80–11.90)     | 11.30 (10.70–11.83)     | 11.25 (10.90–12.20)      | 0.280110                      |
| I.N. Ratio (1.0–1.2 Ratio) median (IQR)                   | 1.00 (1.00–1.10)        | 1.00 (1.00–1.10)        | 1.00 (1.00–1.10)         | 0.342053                      |
| APTT (22–33 Secs) median (IQR)                            | 30.00 (28.00–33.00)     | 30.00 (27.00–32.75)     | 30.00 (28.00–35.00)      | 0.239214                      |
| D-Dimer Quantitative (0.0–0.7 mg/L FEU) median (IQR)      | 0.73 (0.43–1.41)        | 0.72 (0.40–1.34)        | 0.86 (0.59–1.99)         | 0.003815 **                   |
| Urine Analysis  |                         |                         |                          |                               |
| Urine Specific Gravity (1.000–1.030) median (IQR)         | 1.0190 (1.0120–1.0250)  | 1.02 (1.01–1.03)        | 1.02 (1.01–1.02)         | 0.114459                      |
| Urine pH (4.5–8.0)  | 5 (n, %)                | 72 (24.0%)              | 53 (34.6%)               | 19 (45.2%)                    |
|   | 5.5 (n, %)              | 62 (20.7%)              | 49 (32.0%)               | 13 (31.0%)                    |
|   | 6 (n, %)                | 28 (9.3%)               | 25 (16.3%)               | 3 (7.1%)                      |
|   | 6.5 (n, %)              | 14 (4.7%)               | 13 (8.5%)                | 1 (2.4%)                      |
|   | 7 (n, %)                | 15 (5.0%)               | 10 (6.5%)                | 5 (11.9%)                     |
|   | 7.5 (n, %)              | 4 (1.3%)                | 3 (2.0%)                 | 1 (2.4%)                      |
| Urine Protein (Negative) (n, %)                           | Negative                | 92 (30.7%)              | 70 (45.8%)               | 22 (52.4%)                    |
|   | Available               | 103 (34.3%)             | 83 (54.2%)               | 20 (47.6%)                    |
| Urine Glucose (Negative) (n, %)                           | Negative                | 138 (46.0%)             | 110 (71.9%)              | 28 (66.7%)                    |
|   | Available               | 57 (19.0%)              | 43 (28.1%)               | 14 (33.3%)                    |
| Urine Ketone (Negative) (n, %)                            | Negative                | 125 (41.7%)             | 97 (63.4%)               | 28 (66.7%)                    |
|   | Available               | 70 (23.3%)              | 56 (36.6%)               | 14 (33.3%)                    |
| Urine Blood (Negative) (n, %)                             | Negative                | 105 (35.0%)             | 85 (55.6%)               | 20 (47.6%)                    |
|   | Trace                   | 46 (15.3%)              | 34 (22.2%)               | 12 (28.6%)                    |

|   |                                     |           |                         |                         |                          |                                |
|---|-------------------------------------|-----------|-------------------------|-------------------------|--------------------------|--------------------------------|
|   |                                     | Moderate  | 36 (12.0%)              | 29 (19.0%)              | 7 (16.7%)                |                                |
|   |                                     | Numerous  | 8 (2.7%)                | 5 (3.3%)                | 3 (7.1%)                 |                                |
| Urine Bilirubin (Negative) ( <i>n</i> , %)  |                                     | Negative  | 193 (64.3%)             | 152 (99.3%)             | 41 (97.6%)               | 0.385250                       |
|   |                                     | Available | 2 (.7%)                 | 1 (0.7%)                | 1 (2.4%)                 |                                |
| Urine Urobilinogen (0.0–1.0 EU/dL) ( <i>n</i> , %)  |                                     | Normal    | 166 (55.3%)             | 128 (83.7%)             | 38 (90.5%)               | 0.271470                       |
|   |                                     | Abnormal  | 29 (9.7%)               | 25 (16.3%)              | 4 (9.5%)                 |                                |
| Urine Nitrites (Negative) ( <i>n</i> , %)   |                                     | Negative  | 193 (64.3%)             | 151 (98.7%)             | 42 (100.0%)              | 1.000000                       |
|   |                                     | Available | 2 (.7%)                 | 2 (1.3%)                | 0 (0.0%)                 |                                |
| Urine Leuk. Esterase (Negative) ( <i>n</i> , %)   |                                     | Negative  | 182 (60.7%)             | 143 (93.5%)             | 39 (92.9%)               | 1.000000                       |
|   |                                     | Available | 13 (4.3%)               | 10 (6.5%)               | 3 (7.1%)                 |                                |
| Time-related pentameters  |                                     |           |                         |                         |                          |                                |
| Hospital related Parameters   |                                     |           |                         |                         |                          |                                |
| Hospital Length of stay (Days) median (IQR)   |                                     |           | 14.00 (9.00–21.00)      | 13.00 (8.00–19.00)      | 19.00 (14.00–24.00)      | 0.000001 ***                   |
| ICU Related Parameters  |                                     |           |                         |                         |                          |                                |
| ICU Admission   | Not admitted to ICU ( <i>n</i> , %) |           | 139 (46.3%)             | 138 (58.2%)             | 1 (1.6%)                 | 1.1166 × 10 <sup>-15</sup> *** |
|   | Admitted to ICU ( <i>n</i> , %)     |           | 161 (53.7%)             | 99 (41.8%)              | 62 (98.4%)               |                                |
| For patients admitted to ICU: Time between Hospital admission and ICU admission (Days) median (IQR)                           |                                     |           | 3.00 (1.00–5.00)        | 3.12±3.14               | 5.18±4.37                | 0.001355 **                    |
| For All patients, ICU Length of stay (Days) median (IQR)  |                                     |           | 3.00 (0.00–12.00)       | 0.00 (0.00–7.00)        | 14.00 (8.00–21.00)       | 1.0979 × 10 <sup>-18</sup> *** |
| For patients admitted to ICU, ICU Length of stay (Days) median (IQR)  |                                     |           | 11.00 (6.00–18.00)      | 9.00 (4.00–16.00)       | 14.50 (8.00–21.00)       | 0.001845 **                    |
| Tocilizumab Related Parameters  |                                     |           |                         |                         |                          |                                |
| Number of Tocilizumab Doses   |                                     |           |                         |                         |                          |                                |
| Number of Tocilizumab Doses ( <i>n</i> ) median (IQR)   |                                     |           | 2.00 (1.00–2.00)        | 1.00 (1.00–2.00)        | 2.00 (2.00–4.00)         | 1.9903 × 10 <sup>-7</sup> ***  |
| Number of Tocilizumab Doses   | One Dose ( <i>n</i> , %)            |           | 146 (48.7%)             | 133 (56.1%)             | 13 (20.6%)               | 8.9772 × 10 <sup>-8</sup> ***  |
|   | Two Doses ( <i>n</i> , %)           |           | 82 (27.3%)              | 57 (24.1%)              | 25 (39.7%)               |                                |
|   | Three Doses ( <i>n</i> , %)         |           | 36 (12.0%)              | 29 (12.2%)              | 7 (11.1%)                |                                |
|   | Four Doses or more ( <i>n</i> , %)  |           | 36 (12.0%)              | 18 (7.6%)               | 18 (28.6%)               |                                |
| Total Tocilizumab (mg)  |                                     |           |                         |                         |                          |                                |
| Total Tocilizumab (mg) median (IQR)   |                                     |           | 800.00 (400.00–1600.00) | 800.00 (400.00–1200.00) | 1400.00 (800.00–2400.00) | 6.1184 × 10 <sup>-7</sup> ***  |
| Total Tocilizumab (mg)  | <800 ( <i>n</i> , %)                |           | 176 (58.7%)             | 155 (65.4%)             | 21 (33.3%)               | 0.000004 ***                   |
|   | 801–1600 ( <i>n</i> , %)            |           | 69 (23.0%)              | 47 (19.8%)              | 22 (34.9%)               |                                |
|   | 1601–2400 ( <i>n</i> , %)           |           | 27 (9.0%)               | 21 (8.9%)               | 6 (9.5%)                 |                                |
|   | >2401 ( <i>n</i> , %)               |           | 28 (9.3%)               | 14 (5.9%)               | 14 (22.2%)               |                                |
| Total Tocilizumab (mg/Kg) <sup>iii</sup>  |                                     |           |                         |                         |                          |                                |
| Total tocilizumab (mg/kg) median (IQR)  |                                     |           | 9.5125 (5.88–17.60)     | 8.40 (5.56–15.95)       | 16.69 (9.71–29.02)       | 6.0238 × 10 <sup>-7</sup> ***  |
| Total tocilizumab (mg/Kg)   | <10 mg/kg ( <i>n</i> , %)           |           | 159 (53.0%)             | 142 (59.9%)             | 17 (27.0%)               | 0.000003 ***                   |
|   | 10.1–21 mg/kg ( <i>n</i> , %)       |           | 86 (28.7%)              | 61 (25.7%)              | 25 (39.7%)               |                                |
|   | 21.1–32 mg/kg ( <i>n</i> , %)       |           | 27 (9.0%)               | 20 (8.4%)               | 7 (11.1%)                |                                |
|   | >32 mg/kg ( <i>n</i> , %)           |           | 28 (9.3%)               | 14 (5.9%)               | 14 (22.2%)               |                                |
| Time-Related Parameters (All Patients)  |                                     |           |                         |                         |                          |                                |
| Time between admission and first dose of tocilizumab (Days) median (IQR)  |                                     |           | 3.00 (1.00–5.00)        | 2.00 (1.00–4.00)        | 4.00 (2.00–7.00)         | 0.000761 ***                   |
| For patients received the first dose of tocilizumab in ICU: Time between ICU admission and the first dose (Days) median (IQR) |                                     |           | 1.00 (.00–2.00)         | 1.00 (0.00–2.00)        | 1.00 (0.00–3.00)         | 0.030501 *                     |
| ICU length of stay after last dose of tocilizumab (Days) median (IQR)   |                                     |           | 7.00 (4.00–13.00)       | 5.00 (3.00–10.00)       | 8.00 (4.00–15.00)        | 0.011098 *                     |
| Hospital Length of stay after last dose of tocilizumab (Days) median (IQR)  |                                     |           | 8.00 (5.00–13.00)       | 8.00 (5.00–13.00)       | 8.00 (4.00–15.00)        | 0.875129                       |
| Time Related Parameters (Tocilizumab Doses = 2)   |                                     |           |                         |                         |                          |                                |
| Time between first and second dose of tocilizumab (Days) median (IQR)   |                                     |           | 3.00 (2.00–5.00)        | 3.00 (2.00–4.00)        | 4.00 (1.50–7.00)         | 0.152134                       |
| Time Related Parameters (Tocilizumab Doses = 3)   |                                     |           |                         |                         |                          |                                |
| Time between first and second dose of tocilizumab (Days) median (IQR)   |                                     |           | 1.00 (1.00–2.75)        | 1.00 (1.00–2.00)        | 1.00 (1.00–5.00)         | 0.456105                       |
| Time between second and third dose of tocilizumab (Days) median (IQR)   |                                     |           | 1.00 (1.00–3.00)        | 1.00 (1.00–3.00)        | 2.00 (1.00–3.00)         | 0.638697                       |
| Time between first and third dose of tocilizumab (Days) median (IQR)  |                                     |           | 4.00 (2.00–7.00)        | 3.00 (2.00–6.50)        | 7.00 (2.00–7.00)         | 0.269682                       |



\*  $p < 0.05$  is statistically significant; \*\*  $p < 0.01$  is statistically very significant; \*\*\*  $p < 0.001$  is statistically extremely significant; <sup>i</sup> Proportion set at the mortality rate of 16.1% based on the highest mortality rate reported for COVID-19 patients on tocilizumab in Saudi Arabia [4]; <sup>ii</sup> The proportion set at the mortality rate of 31.1% based on the highest mortality reported for ICU COVID-19 patients on tocilizumab in Saudi Arabia [16]; <sup>iii</sup> Calculated based on the average weight of the KSA adult =75 kg.

**Table S5.** Univariate binary logistic regression analysis for mortality in COVID-19 patients on tocilizumab (demographical and clinical characteristics, concurred drug administration, and time & tocilizumab related parameters).

| Parameters   |                                    | ODDs ratio (95% CI)                | p-value                     | Reference Group                             |
|--|------------------------------------|------------------------------------|-----------------------------|---|
| Demographical Characteristics  |                                    |                                    |                             |   |
| Age (year)   |                                    | 1.073 (1.044–1.102)                | 4.4265 × 10 <sup>-7</sup> ¥ |   |
| Gender   | Male                               | .828 (.466–1.472)                  | 0.520329                    | Female                                      |
| Nationality  | Saudi                              | 2.218 (0.496–9.912)                | 0.296941                    | Non-Saudi                                   |
| Weight (Kg) median   |                                    | 0.998 (0.983–1.012)                | 0.742584                    |   |
| Body mass index (Kg/m²)  |                                    | 1.010 (0.975–1.046)                | 0.575646                    |   |
| Body Mass Index category   | Underweight (<18.5)                | 0.000 (0.000–0.000)                | 0.999284                    | Normal weight                               |
|  | Overweight (25.0–29.9)             | 0.298 (0.117–0.762)                | 0.011445¥                   |   |
|  | Obese (>35.0)                      | 0.374 (0.160–0.876)                | 0.023444¥                   |   |
| Smoking status   | Former-smoker                      | 0.518 (0.193–1.390)                | 0.191324                    | Non-smoker                                  |
|  | Active-smoker                      | 1.056 (0.403–2.765)                | 0.912041                    |   |
| Clinical Characteristics   |                                    |                                    |                             |   |
| Number of Comor-bidities   | 1                                  | 1.372 (.530–3.550)                 | 0.513993                    | No comorbidity                              |
|  | 2                                  | 0.939 (0.328–2.691)                | 0.907031                    |   |
|  | 3 or more                          | 4.063(1.809–9.126)                 | 0.000682 ¥                  |   |
| Concurrent Drug Administration   |                                    |                                    |                             |   |
| Patients who received at least one type of antiviral drug  |                                    | 3.031 (1.644–5.587)                | 0.000381 ¥                  | Patients did not receive antiviral drug     |
| Patients who received at least one type of corticosteroids   |                                    | 4.330 × 10 <sup>-8</sup> (0.000–.) | 0.999442                    | Patients did not receive corticosteroid     |
| Patients who received hydroxychloroquine   |                                    | 1.707 (0.904–3.223)                | 0.099353 ¥                  | Patients did not receive hydroxychloroquine |
| Time-related pentameters   |                                    |                                    |                             |   |
| Hospital related Parameters  |                                    |                                    |                             |   |
| Hospital Length of stay (Days)   |                                    | 1.022 (1.006–1.038)                | 0.007188 ¥                  |   |
| ICU Related Parameters   |                                    |                                    |                             |   |
| ICU Admission  | Admitted to ICU                    | 86.424 (11.784–633.822)            | 0.000012 ¥                  | Patients not admitted to ICU                |
| For patients admitted to ICU: Time between hospital admission and ICU admission (Days)                               |                                    | 1.162 (1.056–1.280)                | 0.002186 ¥                  |   |
| For All patients, ICU Length of Stay (Days)  |                                    | 1.094 (1.063–1.127)                | 2.1868 × 10 <sup>-9</sup> ¥ |   |
| For patients admitted to ICU, ICU Length of Stay (Days)  |                                    | 1.039 (1.011–1.068)                | 0.005770 ¥                  |   |
| Tocilizumab Related Parameters   |                                    |                                    |                             |   |
| Number of Tocilizumab Doses  |                                    |                                    |                             |   |
| Number of tocilizumab Doses ( <i>n</i> )   |                                    | 1.434 (1.213–1.696)                | 0.000025 ¥                  | Patients receive one dose                   |
| Number of Tocili-zumab Doses   | Two Doses ( <i>n</i> , %)          | 4.487 (2.144–9.391)                | 0.000068 ¥                  |   |
|  | Three Doses ( <i>n</i> , %)        | 2.469 (0.906–6.732)                | 0.077249 ¥                  |   |
|  | Four Doses or more ( <i>n</i> , %) | 10.231 (4.300–24.340)              | 1.452 × 10 <sup>-7</sup> ¥  |   |
| Total Tocilizumab (mg)   |                                    |                                    |                             |   |
| Total tocilizumab (mg)   |                                    | 1.000 (1.000–1.001)                | 0.000071 ¥                  | Patients receive <800 mg tocilizumab        |
| Total Tocilizumab (mg)   | 801–1600 ( <i>n</i> , %)           | 3.455 (1.748–6.828)                | 0.000361 ¥                  |   |
|  | 1601–2400 ( <i>n</i> , %)          | 2.109 (0.764–5.821)                | 0.149772                    |   |
|  | >2401 ( <i>n</i> , %)              | 7.381 (3.093–17.614)               | 0.000007 ¥                  |   |
| Total Tocilizumab (mg/kg)  |                                    |                                    |                             |   |
| Total tocilizumab (mg/kg)  |                                    | 1.039 (1.020–1.058)                | 0.000047 ¥                  | Patients receive <10 mg/kg tocili-zumab     |
| Total Tocilizumab (mg/Kg)  | 10.1–21 mg/kg                      | 3.423 (1.725–6.793)                | 0.000432 ¥                  |   |
|  | 21.1–32 mg/kg                      | 2.924 (1.079–7.923)                | 0.034936¥                   |   |
|  | >32 mg/k                           | 8.353 (3.412–20.451)               | 0.000003 ¥                  |   |
| Time-Related Parameters (All Patients)   |                                    |                                    |                             |   |
| The time between admission and the first dose of tocilizumab (Days)  |                                    | 1.146 (1.060–1.238)                | 0.000633 ¥                  |   |
| For patients who received the first dose of tocilizumab in ICU: Time between ICU admission and the first dose (Davs) |                                    | 1.085 (0.935–1.259)                | 0.280976                    |   |

|   |                     |                       |
|---|---------------------|-----------------------|
| ICU length of stay after the last dose of tocilizumab (Days)    | 1.065 (1.021–1.111) | 0.003318 <sup>‡</sup> |
| Hospital Length of stay after last dose of tocilizumab (Days)   | 1.004 (0.981–1.028) | 0.722882              |
| Time Related Parameters (Tocilizumab Doses = 2)                 |                     |                       |
| Time between first and second dose of tocilizumab (Days)        | 1.110 (0.9721.268)  | 0.124844              |
| Time Related Parameters (Tocilizumab Doses = 3)                 |                     |                       |
| Time between first and second dose of tocilizumab (Days)        | 1.377 (0.924–2.054) | 0.116403              |
| Time between second and third dose of tocilizumab (Days)        | 1.012 (0.664–1.541) | 0.956609              |
| The time between the first and third dose of tocilizumab (Days) | 1.208 (0.893–1.635) | 0.220946              |

<sup>‡</sup>  $p < 0.1$ .

**Table S6.** Univariate binary logistic regression analysis for mortality in COVID-19 patients on tocilizumab (laboratory results).

| Parameters                                    |           | ODDs ratio (95% CI)      | p-value               | Reference Group                 |
|---|-----------|--------------------------|-----------------------|---------------------------------|
| Laboratory Characteristics                    |           |                          |                       |                                 |
| Electrolytes                                  |           |                          |                       |                                 |
| Sodium (135–145 mEq/L)                        |           | 0.987 (0.920–1.059)      | 0.715092              |                                 |
| Potassium (3.5–5.1 mEq/L)                     |           | 1.602 (0.926–2.770)      | 0.091881 <sup>†</sup> |                                 |
| Calcium (8.6–10.0 mg/dL)                      |           | 1.000 (0.559–1.790)      | 0.998777              |                                 |
| Magnesium (1.7–2.4 mg/dL)                     |           | 2.282 (0.741–7.027)      | 0.150533              |                                 |
| Phosphorus (2.5–4.5 mg/dL)                    |           | 1.406 (1.022–1.934)      | 0.036311 <sup>†</sup> |                                 |
| Chloride (98–107 mEq/L)                       |           | 0.972 (0.925–1.022)      | 0.269471              |                                 |
| Carbon Dioxide (22–28 mEq/L)                  |           | 0.991 (0.925–1.061)      | 0.795548              |                                 |
| Chemical Profile                              |           |                          |                       |                                 |
| Blood Urea Nitrogen (6–20 mg/dL)              |           | 1.040 (1.023–1.057)      | 0.000003 <sup>†</sup> |                                 |
| Creatinine (0.66–1.25 mg/dL)                  |           | 1.243 (1.041–1.485)      | 0.016337 <sup>†</sup> |                                 |
| Blood Glucose Level (73–178 mg/dL))           |           | 0.999 (0.996–1.002)      | 0.545564              |                                 |
| Lactic Acid (0.7–2.1 mmol/L)                  |           | 1.158 (0.788–1.701)      | 0.455904              |                                 |
| Cardiac Profile                               |           |                          |                       |                                 |
| Troponin High Sensitive (0.000–0.026 ng/mL)   |           | 3.375 (0.723–15.752)     | 0.121689              |                                 |
| B-type Natriuretic Peptide (<100 pg/mL)       |           | 1.001 (0.999–1.002)      | 0.416247              |                                 |
| Hepatic Profile                               |           |                          |                       |                                 |
| Bilirubin, Total (0.2–1.3 mg/dL)              |           | 1.601 (0.919–2.789)      | 0.096617 <sup>†</sup> |                                 |
| Alk. Phosphatase (53–128 IU/L)                |           | 1.006 (0.996–1.016)      | 0.273923              |                                 |
| ALT (SGPT) (<50 IU/L)                         |           | 1.000 (0.991–1.010)      | 0.926407              |                                 |
| AST (SGOT) (17–59 IU/L)                       |           | 1.009 (1.002–1.015)      | 0.007706 <sup>†</sup> |                                 |
| LDH (120–246 IU/L)                            |           | 1.001 (1.000–1.003)      | 0.027457 <sup>†</sup> |                                 |
| Iron/Anemia Profile                           |           |                          |                       |                                 |
| Ferritin (21.81–274.66 ng/mL)                 |           | 1.000 (1.000–1.000)      | 0.244069              |                                 |
| CRP, Quantitative                             |           |                          |                       |                                 |
| CRP, Quantitative (<1.0 mg/dL)                |           | 0.992 (0.963–1.022)      | 0.616217              |                                 |
| Complete Blood Count                          |           |                          |                       |                                 |
| WBC (4.0–10.0 K/ $\mu$ L)                     |           | 1.032 (0.969–1.099)      | 0.324512              |                                 |
| RBC (4.5–5.9 M/ $\mu$ L)                      |           | 0.617 (0.423–0.901)      | 0.012322 <sup>†</sup> |                                 |
| Hemoglobin (13.5–17.5 g/dL)                   |           | 0.885 (0.763–1.027)      | 0.107485              |                                 |
| Hematocrit (41–53 %)                          |           | 0.954 (0.905–1.005)      | 0.076490 <sup>†</sup> |                                 |
| MCV (77–96 fL)                                |           | 1.037 (1.002–1.074)      | 0.038423 <sup>†</sup> |                                 |
| MCH (26–34 pg)                                |           | 1.077 (0.990–1.173)      | 0.085384 <sup>†</sup> |                                 |
| MCHC (32–36 g/dL)                             |           | 1.033 (0.865–1.233)      | 0.722060              |                                 |
| RDW (10.9–15.7)                               |           | 1.131 (1.020–1.255)      | 0.019835 <sup>†</sup> |                                 |
| Platelets (150–450 K/ $\mu$ L)                |           | 0.995 (0.992–0.999)      | 0.009737 <sup>†</sup> |                                 |
| Mean Platelet Volume (9.0–13.0 fL)            |           | 1.134 (0.849–1.515)      | 0.394393              |                                 |
| Platelets Distribution Width (10.1–16.1 fL)   |           | 1.081 (0.971–1.204)      | 0.152812              |                                 |
| Neut. Absolute (1.8–7.0 K/ $\mu$ L)           |           | 1.038 (0.967–1.114)      | 0.300239              |                                 |
| Lymph. Absolute (0.9–4.9 K/ $\mu$ L)          |           | 0.411 (0.206–0.821)      | 0.011710 <sup>†</sup> |                                 |
| Mono. Absolute (0.0–1.0 K/ $\mu$ L)           |           | 0.925 (0.411–2.084)      | 0.850539              |                                 |
| Eos. Absolute (0.0–0.4 K/ $\mu$ L)            |           | 0.000 (0.000–123.752)    | 0.144657              |                                 |
| Baso. Absolute (0.0–0.1 K/ $\mu$ L)           |           | 0.000 (0.000–827.380)    | 0.192178              |                                 |
| Band Neutrophil Absolute (0.0–0.5 K/ $\mu$ L) |           | 1.138 (0.582–2.227)      | 0.705807              |                                 |
| Coagulation                                   |           |                          |                       |                                 |
| Prothrombin Time (9.8–12.7 Secs)              |           | 1.035 (0.945–1.135)      | 0.458576              |                                 |
| I.N. Ratio (1.0–1.2 Ratio)                    |           | 1.342 (0.544–3.312)      | 0.523519              |                                 |
| APTT (22–33 Secs)                             |           | 1.047 (0.994–1.102)      | 0.084205 <sup>†</sup> |                                 |
| D-Dimer Quantitative (0.0–0.7 mg/L FEU)       |           | 1.069 (1.024–1.117)      | 0.002427 <sup>†</sup> |                                 |
| Urine Analysis                                |           |                          |                       |                                 |
| Urine Specific Gravity (1.000–1.030)          |           | 0.000 (0.000–12,872.334) | 0.133710              |                                 |
| Urine pH (4.5–8.0)                            | 5.5       | 0.740 (0.331–1.656)      | 0.463803              | pH =5, the highest frequency pH |
|   | 6         | 0.335 (0.091–1.237)      | 0.100818              |                                 |
|   | 6.5       | 0.215 (0.026–1.753)      | 0.150945              |                                 |
|   | 7         | 1.395 (0.422–4.606)      | 0.585162              |                                 |
|   | 7.5       | 0.930 (0.091–9.491)      | 0.951051              |                                 |
| Urine Protein (Negative)                      | Available | 0.767 (0.387–1.519)      | 0.446520              | Urine Protein = Negative        |
| Urine Glucose (Negative)                      | Available | 1.279 (0.615–2.660)      | 0.509882              | Urine Glucose = Negative        |

|                                    |           |                      |          |   |
|------------------------------------|-----------|----------------------|----------|---|
| Urine Ketone (Negative)            | Available | 0.866 (0.421–1.781)  | 0.695876 | Urine Ketone= Negative                      |
|                                    | Trace     | 1.500 (0.661–3.402)  | 0.331744 |   |
| Urine Blood (Negative)             | Moderate  | 1.026 (0.393–2.675)  | 0.958356 | Urine Blood = Negative                      |
|                                    | Numerous  | 2.550 (0.562–11.566) | 0.224955 |   |
| Urine Bilirubin (Negative)         | Available | 3.707 (0.227–60.551) | 0.357867 | Urine Bilirubin (Negative)                  |
| Urine Urobilinogen (0.0–1.0 EU/dL) | Abnormal  | 0.539 (0.177–1.645)  | 0.277593 | Urine Urobilinogen = Normal (0.0–1.0 EU/dL) |
| Urine Nitrites (Negative)          | Available | 0.000 (0.000– .)     | 0.999441 | Urine Nitrites = Negative                   |
| Urine Leuk. Esterase (Negative)    | Available | 1.100 (0.289–4.192)  | 0.888957 | Urine Leuk. Esterase = Negative             |

\* $p < 0.1$ .

**Table S7.** Correlation matrix for multicollinearity check between different mortality predictors in COVID-19 patients on tocilizumab (demographical and clinical characteristics, concurrent drugs administration, and time and tocilizumab related parameters) <sup>ε</sup>.

|                            |          | Age    | BMI    | Comor-<br>bidities | Antiviral | Hy-<br>droxychloro-<br>quine | HLS    | Being in<br>ICU | H.A to<br>ICU.A | ICULS  | NO. OF<br>DOSES | No. of<br>doses four<br>groups | Total mg | Total mg 4<br>groups | Total<br>mg/kg | Total<br>mg/kg 4<br>groups | HA to 1 <sup>st</sup><br>dose | ICULS<br>after the<br>last dose |
|----------------------------|----------|--------|--------|--------------------|-----------|------------------------------|--------|-----------------|-----------------|--------|-----------------|--------------------------------|----------|----------------------|----------------|----------------------------|-------------------------------|---------------------------------|
| Age                        | P. Corr. | 1      | -0.255 | 0.315              | 0.052     | -0.041                       | 0.101  | 0.225           | 0.078           | 0.123  | 0.185           | 0.209                          | 0.157    | 0.219                | 0.226          | 0.267                      | 0.054                         | 0.004                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| BMI                        | P. Corr. | -0.255 | 1      | -0.090             | 0.042     | 0.11                         | -0.071 | -0.014          | -0.107          | -0.083 | -0.019          | -0.018                         | 0.049    | 0.038                | -0.088         | -0.100                     | -0.144                        | -0.221                          |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Comorbidities              | P. Corr. | 0.315  | -0.090 | 1                  | 0.011     | 0.078                        | 0.033  | 0.209           | 0.187           | 0.063  | 0.1             | 0.138                          | 0.068    | 0.105                | 0.095          | 0.088                      | 0.117                         | -0.098                          |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Antiviral                  | P. Corr. | 0.052  | 0.042  | 0.011              | 1         | 0.391                        | 0.311  | 0.435           | -0.041          | 0.335  | 0.159           | 0.135                          | 0.145    | 0.115                | 0.158          | 0.162                      | 0.216                         | 0.051                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Hydroxychloroquine         | P. Corr. | -0.041 | 0.11   | 0.078              | 0.391     | 1                            | 0.198  | 0.233           | -0.023          | 0.145  | -0.135          | -0.111                         | -0.160   | -0.146               | -0.168         | -0.162                     | 0.35                          | -0.020                          |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| HLS                        | P. Corr. | 0.101  | -0.071 | 0.033              | 0.311     | 0.198                        | 1      | 0.42            | 0.155           | 0.804  | 0.452           | 0.458                          | 0.395    | 0.402                | 0.421          | 0.414                      | 0.319                         | 0.688                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Being in ICU               | P. Corr. | 0.225  | -0.014 | 0.209              | 0.435     | 0.233                        | 0.42   | 1               | -0.153          | 0.605  | 0.442           | 0.494                          | 0.395    | 0.437                | 0.408          | 0.449                      | 0.224                         | . <sup>a</sup>                  |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| H.A to ICU.A               | P. Corr. | 0.078  | -0.107 | 0.187              | -0.041    | -0.023                       | 0.155  | -0.153          | 1               | 0.016  | 0.058           | 0.033                          | 0.015    | -0.035               | 0.049          | 0.052                      | 0.441                         | 0.043                           |
|                            | N        | 159    | 159    | 159                | 159       | 159                          | 159    | 159             | 159             | 159    | 159             | 159                            | 159      | 159                  | 159            | 159                        | 159                           | 154                             |
| ICULS                      | P. Corr. | 0.123  | -0.083 | 0.063              | 0.335     | 0.145                        | 0.804  | 0.605           | 0.016           | 1      | 0.537           | 0.559                          | 0.495    | 0.514                | 0.504          | 0.514                      | 0.186                         | 0.89                            |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| NO. OF DOSES               | P. Corr. | 0.185  | -0.019 | 0.1                | 0.159     | -0.135                       | 0.452  | 0.442           | 0.058           | 0.537  | 1               | 0.915                          | 0.957    | 0.899                | 0.959          | 0.889                      | -0.155                        | 0.186                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| No. of doses four groups   | P. Corr. | 0.209  | -0.018 | 0.138              | 0.135     | -0.111                       | 0.458  | 0.494           | 0.033           | 0.559  | 0.915           | 1                              | 0.857    | 0.924                | 0.865          | 0.917                      | -0.131                        | 0.263                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Total mg                   | P. Corr. | 0.157  | 0.049  | 0.068              | 0.145     | -0.160                       | 0.395  | 0.395           | 0.015           | 0.495  | 0.957           | 0.857                          | 1        | 0.912                | 0.96           | 0.873                      | -0.187                        | 0.149                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Total mg 4 groups          | P. Corr. | 0.219  | 0.038  | 0.105              | 0.115     | -0.146                       | 0.402  | 0.437           | -0.035          | 0.514  | 0.899           | 0.924                          | 0.912    | 1                    | 0.893          | 0.919                      | -0.170                        | 0.197                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Total mg/kg                | P. Corr. | 0.226  | -0.088 | 0.095              | 0.158     | -0.168                       | 0.421  | 0.408           | 0.049           | 0.504  | 0.959           | 0.865                          | 0.96     | 0.893                | 1              | 0.914                      | -0.147                        | 0.167                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| Total mg/kg 4 groups       | P. Corr. | 0.267  | -0.100 | 0.088              | 0.162     | -0.162                       | 0.414  | 0.449           | 0.052           | 0.514  | 0.889           | 0.917                          | 0.873    | 0.919                | 0.914          | 1                          | -0.123                        | 0.212                           |
|                            | N        | 300    | 300    | 300                | 300       | 300                          | 300    | 300             | 159             | 300    | 300             | 300                            | 300      | 300                  | 300            | 300                        | 300                           | 154                             |
| HA to 1 <sup>st</sup> dose | P. Corr. | 0.054  | -0.144 | 0.117              | 0.216     | 0.35                         | 0.319  | 0.224           | 0.441           | 0.186  | -0.155          | -0.131                         | -0.187   | -0.170               | -0.147         | -0.123                     | 1                             | 0.057                           |

|                           |          |   |       |        |        |       |        |       |                |       |      |       |       |       |       |       |       |       |     |
|---------------------------|----------|---|-------|--------|--------|-------|--------|-------|----------------|-------|------|-------|-------|-------|-------|-------|-------|-------|-----|
|                           |          | N | 300   | 300    | 300    | 300   | 300    | 300   | 300            | 159   | 300  | 300   | 300   | 300   | 300   | 300   | 300   | 300   | 154 |
| ICULS after the last dose | P. Corr. |   | 0.004 | −0.221 | −0.098 | 0.051 | −0.020 | 0.688 | . <sup>a</sup> | 0.043 | 0.89 | 0.186 | 0.263 | 0.149 | 0.197 | 0.167 | 0.212 | 0.057 | 1   |
|                           | N        |   | 154   | 154    | 154    | 154   | 154    | 154   | 154            | 154   | 154  | 154   | 154   | 154   | 154   | 154   | 154   | 154   | 154 |

<sup>ε</sup>Predictors with absolute correlation coefficients ≥0.7 are considered strongly correlated. <sup>a</sup> Correlation not Calculated

|                  |          | Potassium | Phosphorus | BUN    | Creatinine | Bilirubin, Total | AST    | LDH    | RBC    | Hematocrit | MCV    | MCH    | RDW    | Platelets | Lymph. Absolute | APTT   | D-Dimer |
|------------------|----------|-----------|------------|--------|------------|------------------|--------|--------|--------|------------|--------|--------|--------|-----------|-----------------|--------|---------|
| Potassium        | P. Corr. | 1         | 0.335      | 0.235  | 0.16       | 0.058            | 0.097  | 0.106  | 0.023  | 0.076      | 0.086  | 0.017  | 0.025  | 0.109     | -0.084          | -0.074 | 0.075   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Phosphorus       | P. Corr. | 0.335     | 1          | 0.537  | 0.455      | -0.098           | -0.15  | -0.079 | -0.072 | -0.149     | -0.034 | -0.089 | 0.105  | 0.094     | -0.129          | 0.123  | -0.109  |
|                  | N        | 117       | 117        | 117    | 117        | 117              | 117    | 116    | 117    | 117        | 117    | 117    | 117    | 117       | 117             | 66     | 115     |
| BUN              | P. Corr. | 0.235     | 0.537      | 1      | 0.727      | 0.059            | 0.019  | 0.046  | -0.193 | -0.219     | 0.056  | -0.011 | 0.093  | -0.022    | -0.175          | 0.037  | 0.158   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Creatinine       | P. Corr. | 0.16      | 0.455      | 0.727  | 1          | 0.071            | 0.036  | 0.006  | -0.216 | -0.247     | 0.056  | 0.022  | 0.042  | -0.074    | -0.152          | 0.18   | 0.073   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Bilirubin, Total | P. Corr. | 0.058     | -0.098     | 0.059  | 0.071      | 1                | 0.226  | 0.246  | -0.22  | -0.152     | 0.182  | 0.163  | 0.012  | -0.039    | -0.134          | -0.011 | 0.258   |
|                  | N        | 282       | 117        | 282    | 282        | 282              | 282    | 280    | 282    | 282        | 282    | 282    | 282    | 282       | 282             | 115    | 273     |
| AST              | P. Corr. | 0.097     | -0.15      | 0.019  | 0.036      | 0.226            | 1      | 0.641  | -0.054 | 0.045      | 0.144  | 0.174  | -0.086 | -0.11     | -0.118          | 0.075  | 0.122   |
|                  | N        | 282       | 117        | 282    | 282        | 282              | 282    | 280    | 282    | 282        | 282    | 282    | 282    | 282       | 282             | 115    | 273     |
| LDH              | P. Corr. | 0.106     | -0.079     | 0.046  | 0.006      | 0.246            | 0.641  | 1      | -0.095 | -0.01      | 0.152  | 0.164  | -0.069 | -0.085    | -0.213          | 0.161  | 0.264   |
|                  | N        | 280       | 116        | 280    | 280        | 280              | 280    | 280    | 280    | 280        | 280    | 280    | 280    | 280       | 280             | 114    | 271     |
| RBC              | P. Corr. | 0.023     | -0.072     | -0.193 | -0.216     | -0.22            | -0.054 | -0.095 | 1      | 0.765      | -0.561 | -0.51  | 0.155  | -0.026    | 0.06            | -0.112 | -0.145  |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Hematocrit       | P. Corr. | 0.076     | -0.149     | -0.219 | -0.247     | -0.152           | 0.045  | -0.01  | 0.765  | 1          | 0.089  | 0.113  | -0.229 | -0.089    | 0.096           | -0.182 | -0.164  |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| MCV              | P. Corr. | 0.086     | -0.034     | 0.056  | 0.056      | 0.182            | 0.144  | 0.152  | -0.561 | 0.089      | 1      | 0.941  | -0.5   | -0.067    | 0.008           | -0.037 | 0.043   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| MCH              | P. Corr. | 0.017     | -0.089     | -0.011 | 0.022      | 0.163            | 0.174  | 0.164  | -0.51  | 0.113      | 0.941  | 1      | -0.531 | -0.086    | 0.013           | -0.012 | 0.046   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| RDW              | P. Corr. | 0.025     | 0.105      | 0.093  | 0.042      | 0.012            | -0.086 | -0.069 | 0.155  | -0.229     | -0.5   | -0.531 | 1      | -0.002    | -0.082          | 0.153  | 0.112   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Platelets        | P. Corr. | 0.109     | 0.094      | -0.022 | -0.074     | -0.039           | -0.11  | -0.085 | -0.026 | -0.089     | -0.067 | -0.086 | -0.002 | 1         | 0.267           | -0.009 | 0.025   |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| Lymph. Absolute  | P. Corr. | -0.084    | -0.129     | -0.175 | -0.152     | -0.134           | -0.118 | -0.213 | 0.06   | 0.096      | 0.008  | 0.013  | -0.082 | 0.267     | 1               | -0.1   | -0.077  |
|                  | N        | 300       | 117        | 300    | 300        | 282              | 282    | 280    | 300    | 300        | 300    | 300    | 300    | 300       | 300             | 119    | 289     |
| APTT             | P. Corr. | -0.074    | 0.123      | 0.037  | 0.18       | -0.011           | 0.075  | 0.161  | -0.112 | -0.182     | -0.037 | -0.012 | 0.153  | -0.009    | -0.1            | 1      | 0.002   |
|                  | N        | 119       | 66         | 119    | 119        | 115              | 115    | 114    | 119    | 119        | 119    | 119    | 119    | 119       | 119             | 119    | 115     |
| D-Dimer          | P. Corr. | 0.075     | -0.109     | 0.158  | 0.073      | 0.258            | 0.122  | 0.264  | -0.145 | -0.164     | 0.043  | 0.046  | 0.112  | 0.025     | -0.077          | 0.002  | 1       |
|                  | N        | 289       | 115        | 289    | 289        | 273              | 273    | 271    | 289    | 289        | 289    | 289    | 289    | 289       | 289             | 115    | 289     |

<sup>‡</sup>Predictors with absolute correlation coefficients  $\geq 0.7$  are considered strongly correlated.

**Table S9.** Multivariable binary logistic regression models for mortality in COVID-19 patients on tocilizumab (Model set A—all data).

Age, BMI-group, number of comorbidities, antiviral drugs administration, hydroxychloroquine administration, hospital length of stay, admission to ICUs, days between hospital admission and the first dose of tocilizumab, number of tocilizumab doses, number of tocilizumab doses-groups, total tocilizumab doses(mg), total tocilizumab doses (mg)-group, total tocilizumab doses (mg/kg), and total tocilizumab doses (mg/kg)-group

| Model Number    | Tocilizumab Presentation               | MODEL  | B-value      | WALD    | ODDs ratio (95% CI)    | Constant of the Model | -2 log-likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p-value | Model Accuracy |
|-----------------|--|--|--------------|---------|------------------------|-----------------------|-------------------|---------------------------|------------------------------|----------------|
| I               | Number of tocilizumab doses            | Age  | 0.078        | 19.775  | 1.081 (1.045–1.119)    | -10.541               | 199.613           | 0.473                     | 0.970                        | 83.7           |
|                 |  | Admitted to ICU                                    | 4.467        | 18.123  | 87.077(11.137–680.806) |                       |                   |                           |                              |                |
|                 |  | Days between hospital admission and the first dose | 0.102        | 4.718   | 1.107 (1.010–1.214)    |                       |                   |                           |                              |                |
| II <sup>‡</sup> | Tocilizumab doses in groups            | Admitted to ICU                                    | 4.169        | 15.728  | 64.644 (8.236–507.365) | -10.401               | 185.330           | 0.524                     | 0.844                        | 84.7           |
|                 |  | Age  | 0.070        | 14.223  | 1.073 (1.034–1.113)    |                       |                   |                           |                              |                |
|                 |  | No. of tocilizumab doses–                          |              |         |                        |                       |                   |                           |                              |                |
|                 |  | Two doses  | 1.387        | 7.363   | 4.005 (1.470–10.910)   |                       |                   |                           |                              |                |
|                 |  | Three doses  | 0.429        | 0.478   | 1.536 (.455–5.189)     |                       |                   |                           |                              |                |
|                 |  | Four doses   | 1.976        | 9.422   | 7.217 (2.043–25.494)   |                       |                   |                           |                              |                |
|                 |  | Days between hospital admission and the first dose | 0.178        | 9.583   | 1.195 (1.068–1.338)    |                       |                   |                           |                              |                |
| III             | (Total tocilizumab in mg) <sup>2</sup> | Hospital length of stay                            | -0.026–      | 3.742   | .974 (.949–1.000)      | -10.541               | 199.613           | 0.473                     | 0.970                        | 83.7           |
|                 |  | Age  | 0.078        | 19.775  | 1.081 (1.045–1.119)    |                       |                   |                           |                              |                |
|                 |  | Admitted to ICU                                    | 4.467        | 18.123  | 87.077(11.137–680.806) |                       |                   |                           |                              |                |
| IV              | Total mg of tocilizumab in groups      | Days between hospital admission and the first dose | 0.102        | 4.718   | 1.107 (1.010–1.214)    | -10.316               | 185.711           | 0.523                     | 0.548                        | 85.7           |
|                 |  | Admitted to ICU                                    | 4.129        | 15.043  | 62.137 (7.711–500.723) |                       |                   |                           |                              |                |
|                 |  | Age  | 0.069        | 13.766  | 1.071 (1.033–1.111)    |                       |                   |                           |                              |                |
|                 |  | Days between hospital admission and the first dose | 0.150        | 8.223   | 1.162 (1.049–1.287)    |                       |                   |                           |                              |                |
|                 |  | Total mg of tocilizumab in groups                  | 801–1600 mg  | 1.016   | 4.770                  |                       |                   |                           |                              |                |
|                 |  |  | 1601–2400 mg | 0.002   | 0.000                  |                       |                   |                           |                              |                |
|                 |  |  | >2401 mg     | 1.236   | 4.983                  |                       |                   |                           |                              |                |
|                 |  | Number of comorbidities                            | 1            | -0.230– | 0.148                  |                       |                   |                           |                              |                |
|                 |  |  | 2            | -0.882– | 1.834                  |                       |                   |                           |                              |                |



|    |   |   |       |        |                        |         |         |       |       |      |
|----|---|---|-------|--------|------------------------|---------|---------|-------|-------|------|
|    |   | 3 or more   | 0.443 | 0.733  | 1.558 (0.565–4.295)    |         |         |       |       |      |
| V  | Total tocili-<br>zumab mg/kg              | Age   | 0.078 | 19.775 | 1.081 (1.045–1.119)    | –10.541 | 199.613 | 0.473 | 0.970 | 83.7 |
|    |   | Admitted to ICU                                       | 4.467 | 18.123 | 87.077(11.137–680.806) |         |         |       |       |      |
|    |   | Days between hospital admission<br>and the first dose | 0.102 | 4.718  | 1.107 (1.010–1.214)    |         |         |       |       |      |
|    |   |   |       |        |                        |         |         |       |       |      |
| VI | Total tocili-<br>zumab mg/kg<br>in groups | Age   | 0.078 | 19.775 | 1.081 (1.045–1.119)    | –10.541 | 199.613 | 0.473 | 0.970 | 83.7 |
|    |   | Admitted to ICU                                       | 4.467 | 18.123 | 87.077(11.137–680.806) |         |         |       |       |      |
|    |   | Days between hospital admission<br>and the first dose | 0.102 | 4.718  | 1.107 (1.010–1.214)    |         |         |       |       |      |
|    |   |   |       |        |                        |         |         |       |       |      |

‡The best model.

**Table S10.** Multivariable binary logistic regression model for mortality in COVID-19 patients on tocilizumab (Model set B—all data).

| Lab results                      |         |       |                     |                       |                   |                           |                              |                |
|----------------------------------|---------|-------|---------------------|-----------------------|-------------------|---------------------------|------------------------------|----------------|
| Variables                        | B-value | WALD  | ODDs ratio (95% CI) | Constant of the Model | −2 log-likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p-value | Model Accuracy |
| D-Dimer Quantitative             | 0.117   | 8.934 | 1.124 (1.041–1.214) | 0.096                 | 121.618           | 0.572                     | 0.454                        | 76.3           |
| 1/ blood phosphate concentration | −4.891  | 3.374 | 0.008 (0.000–1.388) |                       |                   |                           |                              |                |

**Table S11.** AIC values for multivariable binary logistic regression models for mortality in COVID-19 patients on tocilizumab (Model set A—all data).

| Model number     | Calculated AIC <sup>ε</sup> |
|------------------|-----------------------------|
| I, III, and V–VI | 207.613                     |
| II <sup>¥</sup>  | 201.33 <sup>ε</sup>         |
| IV               | 205.711 <sup>ε</sup>        |

<sup>¥</sup>The best model. <sup>ε</sup>Significant differences between models I, III, & V–VI vs. II, and II vs. IV using AIC statistics. No significant difference between models I, III, & V–VI vs. model IV using AIC statistics.

**Table S12.** Multivariable binary logistic regression model for mortality in COVID-19 patients on tocilizumab (Model set B—all data without blood phosphate concentration).

| Lab results          |         |        |                     |                       |                   |                           |                              |                |
|----------------------|---------|--------|---------------------|-----------------------|-------------------|---------------------------|------------------------------|----------------|
| MODEL                | B-value | WALD   | ODDs ratio (95% CI) | Constant of the Model | −2 log-likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p-value | Model Accuracy |
| RDW                  | 0.230   | 10.673 | 1.259 (1.096–1.445) | −8.730                | 239.249           | 0.211                     | 0.449                        | 81.2           |
| MCV                  | 0.051   | 5.517  | 1.052 (1.008–1.098) |                       |                   |                           |                              |                |
| AST                  | 0.007   | 5.227  | 1.007 (1.001–1.014) |                       |                   |                           |                              |                |
| D-Dimer Quantitative | 0.053   | 5.203  | 1.055 (1.008–1.104) |                       |                   |                           |                              |                |
| Platelets            | −0.004  | 4.408  | 0.996 (0.992–1.000) |                       |                   |                           |                              |                |
| Creatinine           | 0.173   | 3.239  | 1.189 (0.985–1.435) |                       |                   |                           |                              |                |

**Table S13.** Multivariable binary logistic regression models for mortality in COVID-19 patients on tocilizumab (Model set A–no outliers).

Age, BMI–group, number of comorbidities, antiviral drugs administration, hydroxychloroquine administration, hospital length of stay, admission to ICUs, days between hospital admission and the first dose of tocilizumab, number of tocilizumab doses, number of tocilizumab doses–groups, total tocilizumab doses(mg), total tocilizumab doses (mg)–group, total tocilizumab doses (mg/kg), and total tocilizumab doses (mg/kg)–group

| Model Number   | Tocilizumab Presentation    | MODEL  | B–value     | WALD    | ODDs ratio (95% CI)    | Constant of the Model | –2 log–likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p–vare | Model Accuracy |
|----------------|-----------------------------|--|-------------|---------|------------------------|-----------------------|-------------------|---------------------------|-----------------------------|----------------|
| 1              | Number of tocilizumab doses | Age  | 0.081       | 15.281  | 1.085 (1.041–1.130)    | –11.324               | 156.488           | 0.572                     | 0.796                       | 87.2           |
|                |                             | Days between hospital admission and the first dose | 0.294       | 13.651  | 1.341 (1.148–1.567)    |                       |                   |                           |                             |                |
|                |                             | Admitted to ICU                                    | 3.947       | 13.533  | 51.800 (6.323–424.335) |                       |                   |                           |                             |                |
|                |                             | Number of comorbidities                            | 1           | –0.453– | 0.456                  |                       |                   |                           |                             |                |
|                |                             |  | 2           | –1.309– | 2.888                  |                       |                   |                           |                             |                |
|                |                             |  | 3 or more   | 0.251   | 0.184                  |                       |                   |                           |                             |                |
|                |                             | Number of tocilizumab doses                        |             | 0.435   | 5.910                  |                       |                   |                           |                             |                |
|                |                             | Hospital length of stay                            |             | –0.035– | 3.624                  |                       |                   |                           |                             |                |
| 2              | Tocilizumab doses in groups | Antiviral drug                                     | 0.793       | 2.948   | 2.209 (0.894–5.461)    | –11.162               | 156.833           | 0.571                     | 0.875                       | 86.8           |
|                |                             | Admitted to ICU                                    | 4.251       | 15.924  | 70.187 (8.699–566.309) |                       |                   |                           |                             |                |
|                |                             | Days between hospital admission and the first dose | 0.310       | 15.142  | 1.363 (1.166–1.593)    |                       |                   |                           |                             |                |
|                |                             | Age  | 0.076       | 13.494  | 1.079 (1.036–1.123)    |                       |                   |                           |                             |                |
|                |                             | No. of tocilizumab doses–groups                    | Two doses   | 1.629   | 8.564                  |                       |                   |                           |                             |                |
|                |                             |  | Three doses | 0.653   | 1.001                  |                       |                   |                           |                             |                |
|                |                             |  | Four doses  | 2.422   | 10.608                 |                       |                   |                           |                             |                |
|                |                             | Hospital length of stay                            |             | –0.041– | 4.865                  |                       |                   |                           |                             |                |
| 3 <sup>y</sup> | Total tocilizumab in mg     | Age  | 0.082       | 15.457  | 1.085 (1.042–1.131)    | –11.244               | 156.380           | 0.573                     | 0.927                       | 87.2           |
|                |                             | Admitted to ICU                                    | 3.986       | 13.821  | 53.852 (6.584–440.442) |                       |                   |                           |                             |                |
|                |                             | Days between hospital admission and the first dose | 0.291       | 13.580  | 1.338 (1.146–1.562)    |                       |                   |                           |                             |                |
|                |                             | Number of comorbidities                            | 1           | –0.569– | 0.716                  |                       |                   |                           |                             |                |
|                |                             |  | 2           | –1.272– | 2.809                  |                       |                   |                           |                             |                |
|                |                             |  | 3 or more   | 0.206   | 0.123                  |                       |                   |                           |                             |                |
|                |                             | Total tocilizumab in mg                            |             | 0.001   | 6.102                  |                       |                   |                           |                             |                |
|                |                             |  |             |         | 1.001 (1.000–1.001)    |                       |                   |                           |                             |                |

|   |                                    |  |              |        |        |                        |         |         |       |       |      |
|---|------------------------------------|--|--------------|--------|--------|------------------------|---------|---------|-------|-------|------|
| 4 | Total mg of to-cilizumab in groups | Hospital length of stay                            |              | −0.030 | 2.888  | 0.971 (0.938–1.005)    | −10.729 | 158.273 | 0.566 | 0.797 | 87.2 |
|   |                                    | Antiviral drug                                     |              | 0.781  | 2.885  | 2.183 (0.887–5.374)    |         |         |       |       |      |
|   |                                    | Admitted to ICU                                    |              | 4.172  | 14.894 | 64.875 (7.795–39.973)  |         |         |       |       |      |
|   |                                    | Age  |              | 0.071  | 12.665 | 1.074 (1.033–1.117)    |         |         |       |       |      |
|   |                                    | Days between hospital admission and the first dose |              | 0.266  | 12.662 | 1.305 (1.127–1.511)    |         |         |       |       |      |
|   |                                    | Number of comorbidities                            | 1            | −0.374 | 7.364  | 0.330                  |         |         |       |       |      |
|   |                                    |  | 2            | −1.454 |        | 3.633                  |         |         |       |       |      |
|   |                                    |  | 3 or more    | 0.228  |        | 0.158                  |         |         |       |       |      |
|   |                                    | Total mg of to-cilizumab in groups                 | 801–1600 mg  | 1.028  | 6.984  | 4.438                  |         |         |       |       |      |
|   |                                    |  | 1601–2400 mg | 0.132  |        | 0.043                  |         |         |       |       |      |
|   |                                    |  | >2401 mg     | 1.380  |        | 4.212                  |         |         |       |       |      |
| 5 | Total tocilizumab mg/kg            | Admitted to ICU                                    |              | 4.335  | 17.020 | 76.341 (9.734–598.725) | −10.690 | 165.513 | 0.539 | 0.736 | 85.4 |
|   |                                    | Age  |              | 0.079  | 15.797 | 1.082 (1.041–1.125)    |         |         |       |       |      |
|   |                                    | Days between hospital admission and the first dose |              | 0.213  | 9.845  | 1.237 (1.083–1.414)    |         |         |       |       |      |
|   |                                    | Number of comorbidities                            | 1            | −0.354 | 6.685  | 0.308                  |         |         |       |       |      |
|   |                                    |  | 2            | −1.302 |        | 3.048                  |         |         |       |       |      |
|   |                                    |  | 3 or more    | 0.233  |        | 0.172                  |         |         |       |       |      |
|   |                                    | Admitted to ICU                                    |              | 4.335  | 17.020 | 76.341 (9.734–598.725) |         |         |       |       |      |
| 6 | Total tocilizumab mg/kg in groups  | Age  |              | 0.079  | 15.797 | 1.082 (1.041–1.125)    | −10.690 | 165.513 | 0.539 | 0.736 | 85.4 |
|   |                                    | Days between hospital admission and the first dose |              | 0.213  | 9.845  | 1.237 (1.083–1.414)    |         |         |       |       |      |
|   |                                    | Number of comorbidities                            | 1            | −0.354 | 6.685  | 0.308                  |         |         |       |       |      |
|   |                                    |  | 2            | −1.302 |        | 3.048                  |         |         |       |       |      |
|   |                                    |  | 3 or more    | 0.233  |        | 0.172                  |         |         |       |       |      |

‡The best model.

**Table S14.** AIC values for multivariable binary logistic regression models for mortality in COVID-19 patients on tocilizumab (Model set A–no outliers).

| Model Number    | Calculated AIC <sup>€</sup> |
|-----------------|-----------------------------|
| I               | 176.488                     |
| II <sup>¥</sup> | 172.833                     |
| III             | 176.380                     |
| IV              | 178.273                     |
| V–VI            | 179.513                     |

<sup>¥</sup>The best model. <sup>€</sup>Significant differences between models I vs. II, I vs. V–VI, II vs. III, II vs. IV, II vs. V–VI, and III vs. V–VI using AIC statistics. There is no significant difference between models I vs. III, I vs. IV, III vs. IV, and IV vs. V–VI using AIC statistics.

**Table S15.** Multivariable binary logistic regression model for mortality in COVID-19 patients on tocilizumab (Model set B–all data–no outliers).

| Lab Results                   |         |       |                       |                       |                   |                           |                             |                |
|-------------------------------|---------|-------|-----------------------|-----------------------|-------------------|---------------------------|-----------------------------|----------------|
| Variables                     | B–value | WALD  | ODDs ratio (95% CI)   | Constant of the Model | –2 log–likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p–vale | Model Accuracy |
| Blood phosphate concentration | 0.801   | 6.937 | 2.227 (1.1.227–4.042) | –4.059                | 90.631            | 0.134                     | 0.073                       | 78.4           |

**Table S16.** Multivariate logistic regression models for mortality in COVID-19 patients on tocilizumab (Model set B–no outliers without blood phosphate concentration).

| Lab Results |         |       |                     |                       |                   |                           |                             |                |
|-------------|---------|-------|---------------------|-----------------------|-------------------|---------------------------|-----------------------------|----------------|
| MODEL       | B–value | WALD  | ODDs ratio (95% CI) | Constant of the Model | –2 log–likelihood | Nagelkerke R <sup>2</sup> | Hosmer And Leme-show p–vale | Model Accuracy |
| RDW         | 0.213   | 5.836 | 1.237 (1.041–1.470) | –8.745                | 197.682           | 0.126                     | 0.350                       | 81.4           |
| Creatinine  | 0.579   | 5.747 | 1.785 (1.111–2.866) |                       |                   |                           |                             |                |
| MCV         | 0.057   | 5.422 | 1.059 (1.009–1.111) |                       |                   |                           |                             |                |
| Platelets   | –0.005– | 4.140 | 0.995 (.990–1.000)  |                       |                   |                           |                             |                |

**Table S17.** Clinical and laboratory characteristics of COVID-19 patients who received single dose of tocilizumab and were discharged alive – the most recent lab results before tocilizumab administration vs. the most recent lab results before discharge (patients discharged alive  $n = 133$ ).

| Parameters   | Value                  |
|--|------------------------|
| Number of patients ( $n$ , %)  | 133 (44.3%)            |
| Tocilizumab Related Parameters   |                        |
| Total Tocilizumab (mg) median (IQR)  | 400.00 (400.00–600.00) |
| Total Tocilizumab (mg/kg) (mean $\pm$ SD)  | 5.88 (5.00–7.45)       |
| Demographical Characteristics  |                        |
| Age median (IQR)   | 58.00 (53.00–67.00)    |
| Gender   |                        |
| Male ( $n$ , %)  | 84 (63.2%)             |
| Female ( $n$ , %)  | 49 (36.8%)             |
| Nationality  |                        |
| Saudi ( $n$ , %)   | 121 (91.0%)            |
| Non-Saudi ( $n$ , %)   | 11 (8.3%)              |
| Weight Related Parameters  |                        |
| Weight median (kg) (IQR)   | 81.50 (74.25–96.00)    |
| Body mass index median (kg/m <sup>2</sup> ) (IQR)  | 31.24 (27.26–35.16)    |
| Body Mass Index category   |                        |
| Underweight (<18.5) ( $n$ , %)   | 1 (0.8%)               |
| Normal weight (18.5–24.9) ( $n$ , %)   | 9 (6.8%)               |
| Overweight (25.0–29.9) ( $n$ , %)  | 45 (33.8%)             |
| Obese (>35.0) ( $n$ , %)   | 48 (58.6%)             |
| Smoking status   |                        |
| Non-smoker ( $n$ , %)  | 101 (75.9%)            |
| Former-smoker ( $n$ , %)   | 21 (15.8%)             |
| Active-smoker ( $n$ , %)   | 11 (8.3%)              |
| Clinical Characteristics   |                        |
| Number of Comorbidities  |                        |
| 0 ( $n$ , %)   | 37 (27.8%)             |
| 1 ( $n$ , %)   | 32 (24.1%)             |
| 2 ( $n$ , %)   | 32 (24.1%)             |
| 3 or more ( $n$ , %)   | 32 (24.1%)             |
| Concurrent Drug Administration   |                        |
| Patients received at least one Antiviral drug ( $n$ , %)   | 15 (11.3%)             |
| Patient received at least one type of Corticosteroids ( $n$ , %)   | 131 (98.5)             |
| Patient received Hydroxychloroquine ( $n$ , %)   | 27 (20.3%)             |
| Time Related Parameters  |                        |
| Hospital Related Parameters  |                        |
| Hospital Length of stay median (IQR)   | 10.00 (6.00–15.00)     |
| ICU Related Parameters   |                        |
| Not admitted to ICU ( $n$ , %)   | 99 (74.4%)             |
| Admitted to ICU ( $n$ , %)   | 34 (25.6)              |
| For patients admitted to ICU: Days between Hospital admission and ICU admission median (IQR)                               | 3.00 (.75–4.25)        |
| ICU Length of stay median (IQR)  | 0.00 (0.00–1.50)       |
| Time Related Parameters–Tocilizumab (All Patients)   |                        |
| The time between admission and the first dose of Tocilizumab median (IQR)  | 3.00 (1.00–4.50)       |
| For patients who received the first dose of Tocilizumab in ICU: Time between ICU admission and the first dose median (IQR) | 1.00 (0.00–3.00)       |
| ICU length of stay after the last dose of Tocilizumab median (IQR)   | 5.00 (3.00–9.50)       |
| Hospital Length of stay after the last dose of Tocilizumab median (IQR)  | 7.00 (5.00–11.00)      |

| Laboratory Characteristics                                |  |  |          |                               |
|---|--|--|----------|-------------------------------|
| Parameter   | Most recent lab result before TCZ administration | Most recent Lab results before discharge | <i>n</i> | <i>p</i> -value               |
| Electrolytes  |  |  |          |                               |
| Sodium (135–145 mEq/L) median (IQR)                       | 136.00 (134.00–138.00)                           | 135.00 (133.00–137.00)                   | 128      | 0.116919                      |
| Potassium (3.5–5.1 mEq/L (mean ± SD)                      | 4.33±0.46  | 4.34±0.45                                | 128      | 0.779753                      |
| Calcium (8.6–10.0 mg/dL ) (mean ± SD)                     | 8.26±0.68  | 8.68±0.58↑                               | 31       | 0.000193 ***                  |
| Magnesium (1.7–2.4 mg/dL) median (IQR)                    | 2.10 (1.90–2.20)                                 | 2.10 (2.00–2.20)                         | 40       | 0.144292                      |
| Phosphorus (2.5–4.5 mg/dL) median (IQR)                   | 3.40 (3.00–3.80)                                 | 3.85 (3.40–4.50)↑                        | 30       | 0.009330 **                   |
| Chloride (98–107 mEq/L) median (IQR)                      | 101.00 (98.00–104.00)                            | 101.00 (98.00–103.00)                    | 128      | 0.839649                      |
| Carbon Dioxide (22–28 mEq/L) median (IQR)                 | 25.00 (23.00–27.00)                              | 26.00 (24.00–29.00)↑                     | 128      | 0.000019 ***                  |
| Chemical Profile  |  |  |          |                               |
| Blood Urea Nitrogen (6–20 mg/dL) median (IQR)             | 17.00 (12.50–23.50)                              | 20.00 (16.00–25.00)↑                     | 128      | 4.4332 × 10 <sup>−7</sup> *** |
| Creatinine (0.66–1.25 mg/dL) median (IQR)                 | 0.8000 (0.6000–0.9000)                           | 0.7000 (0.6000–0.9000)                   | 128      | 0.840693                      |
| Blood Glucose Level (73–178 mg/dL) (mean ± SD)            | 139.00 (107.00–211.00)                           | 171.00 (105.75–262.75)                   | 7        | 0.463071                      |
| Lactic Acid (0.7–2.1 mmol/L) median (IQR)                 | 1.50 (1.20–2.00)                                 | 1.40 (1.10–1.90)                         | 33       | 0.051830                      |
| Cardiac Profile   |  |  |          |                               |
| Troponin High Sensitive (0.000–0.026 ng/mL ) median (IQR) | 0.0060 (0.0030–0.0125)                           | 0.0040 (0.0030–0.0140)                   | 11       | 0.179688                      |
| B-type Natriuretic Peptide (<100 pg/mL) median (IQR)      | 40.70 (17.98–107.15)                             | 48.50 (11.35–133.93)                     | 10       | 0.343750                      |
| Hepatic Profile   |  |  |          |                               |
| Bilirubin, Total (0.2–1.3 mg/dL) median (IQR)             | 0.5000 (.4000–0.7000)                            | 0.5000 (0.3000–0.7000)                   | 90       | 0.105192                      |
| Alk. Phosphatase (53–128 IU/L) median (IQR)               | 67.50 (56.00–87.75)                              | 67.00 (55.50–82.00)                      | 90       | 0.073140                      |
| ALT (SGPT) (<50 IU/L) median (IQR)                        | 32.00 (22.00–49.75)                              | 46.00 (28.75–69.25)↑                     | 90       | 0.038166 *                    |
| AST (SGOT) (17–59 IU/L) median (IQR)                      | 42.50 (33.25–59.00)                              | 40.50 (27.00–53.00)↓                     | 90       | 0.003996 **                   |
| LDH (120–246 IU/L) median (IQR)                           | 316.00 (261.00–407.00)                           | 294.00 (226.75–373.75)↓                  | 89       | 0.010959 *                    |
| Iron/Anemia Profile                                       |  |  |          |                               |
| Ferritin (21.81–274.66 ng/mL) median (IQR)                | 636.00 (349.50–1212.25)                          | 678.50 (358.00–1084.25)                  | 32       | 0.719438                      |
| CRP, Quantitative   |  |  |          |                               |
| CRP, Quantitative (<1.0 mg/dL) median (IQR)               | 13.90 (5.73–19.23)                               | 1.40 (.60–2.50)↓                         | 124      | 2.299 × 10 <sup>−28</sup> *** |
| Complete Blood Count                                      |  |  |          |                               |
| WBC (4.0–10.0 K/μL) median (IQR)                          | 7.30 (5.35–10.10)                                | 7.40 (5.20–9.70)                         | 131      | 0.575072                      |
| RBC (4.5–5.9 M/μL) median (IQR)                           | 4.79 (4.29–5.21)                                 | 4.77 (4.41–5.23)                         | 131      | 0.250536                      |
| Hemoglobin (13.5–17.5 g/dL) median (IQR)                  | 12.30 (11.25–13.70)                              | 12.60 (11.10–13.60)↑                     | 131      | 0.048373 *                    |
| Hematocrit (41–53 %) median (IQR)                         | 38.30 (35.05–42.10)                              | 39.30 (35.80–42.10)↑                     | 131      | 0.048495 *                    |
| MCV (77–96 fL) median (IQR)                               | 82.50 (74.00–87.70)                              | 82.70 (75.50–88.00)                      | 131      | 0.254213                      |
| MCH (26–34 pg) median (IQR)                               | 26.80 (22.95–29.10)                              | 26.90 (23.10–29.20)                      | 131      | 0.926025                      |
| MCHC (32–36 g/dL) median (IQR)                            | 32.40 (31.20–33.35)                              | 32.20 (31.10–33.60)                      | 131      | 0.407383                      |
| RDW (10.9–15.7) median (IQR)                              | 13.80 (12.70–14.80)                              | 13.70 (12.80–15.70)                      | 131      | 0.174452                      |
| Platelets (150–450 K/μL) median (IQR)                     | 242.00 (197.50–321.00)                           | 317.00 (245.00–407.00)↑                  | 131      | 4.883 × 10 <sup>−9</sup> ***  |
| Mean Platelet Volume (9.0–13.0 fL) median (IQR)           | 10.60 (9.70–11.35)                               | 10.40 (9.70–11.10)↓                      | 116      | 0.005262 **                   |

|  |                        |                         |     |                              |
|--|------------------------|-------------------------|-----|------------------------------|
| Platelets Distribution Width (10.1–16.1 fL) median (IQR)   | 12.30 (10.85–14.50)    | 12.05 (10.60–13.90)     | 116 | 0.227170                     |
| Neut. Absolute (1.8–7.0 K/ $\mu$ L) median (IQR)           | 5.80 (3.85–7.95)       | 5.00 (3.10–7.10)↓       | 127 | 0.031823*                    |
| Lymph. Absolute (0.9–4.9 K/ $\mu$ L) median (IQR)          | 0.9000 (0.6000–1.2000) | 1.3000 (.9000–2.0000)↑  | 127 | $1.0634 \times 10^{-11}$ *** |
| Mono. Absolute (0.0–1.0 K/ $\mu$ L) median (IQR)           | 0.3000 (0.2000–0.5000) | 0.5000 (0.4000–0.8000)↑ | 127 | $3.6741 \times 10^{-12}$ *** |
| Eos. Absolute (0.0–0.4 K/ $\mu$ L) median (IQR)            | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.1000)↑ | 126 | $1.2978 \times 10^{-9}$ ***  |
| Baso. Absolute (0.0–0.1 K/ $\mu$ L) median (IQR)           | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000)  | 126 | 0.404873                     |
| Band Neutrophil Absolute (0.0–0.5 K/ $\mu$ L) median (IQR) | 0.2550 (0.1000–0.5775) | 0.2300 (0.1300–0.4625)  | 21  | 1.000000                     |
| Coagulation  |                        |                         |     |                              |
| Prothrombin Time (9.8–12.7 Secs) median (IQR)              | 11.30 (10.70–11.90)    | 11.80 (11.17–12.62)     | 17  | 0.301758                     |
| I.N. Ratio (1.0–1.2 Ratio) median (IQR)                    | 1.00 (1.00–1.10)       | 1.10 (1.00–1.10)        | 17  | 0.218750                     |
| APTT (22–33 Secs) median (IQR)                             | 29.00 (27.00–33.00)    | 27.00 (25.00–28.75)     | 13  | 0.092285                     |
| D–Dimer Quantitative (0.0–0.7 mg/L FEU) median (IQR)       | 0.65 (0.36–1.15)       | 0.79 (0.40–1.40)        | 104 | 0.768625                     |
| Urine Analysis   |                        |                         |     |                              |
| Urine Specific Gravity (1.000–1.030) (mean $\pm$ SD)       | 1.0233 $\pm$ .0121     | 1.0213 $\pm$ .00300     | 9   | 0.688328                     |
| Urine pH (4.5–8.0)   | 5 (n, %)               |                         | 9   | 0.432768                     |
|  | 5.5 (n, %)             |                         |     |                              |
|  | 6 (n, %)               |                         |     |                              |
|  | 6.5 (n, %)             |                         |     |                              |
|  | 7 (n, %)               |                         |     |                              |
|  | 7.5 (n, %)             |                         |     |                              |
| Urine Protein (Negative) (n)                               | Negative               | 1                       | 9   | 0.500000                     |
|  | Available              | 8                       |     |                              |
| Urine Glucose (Negative) (n)                               | Negative               | 8                       | 9   | 1.000000                     |
|  | Available              | 1                       |     |                              |
| Urine Ketone (Negative) (n)                                | Negative               | 5                       | 9   | 0.500000                     |
|  | Available              | 4                       |     |                              |
| Urine Blood (Negative) (n)                                 | Negative               |                         | 9   | 0.763025                     |
|  | Trace                  |                         |     |                              |
|  | Moderate               |                         |     |                              |
|  | Numerous               |                         |     |                              |
| Urine Bilirubin (Negative) (n)                             | Negative               | 9                       | 9   | 1.000000                     |
|  | Available              | 0                       |     |                              |
| Urine Urobilinogen (0.0–1.0 EU/dL) (n)                     | Normal                 | 7                       | 9   | 0.500000                     |
|  | Abnormal               | 2                       |     |                              |
| Urine Nitrites (Negative) (n)                              | Negative               | 9                       | 9   | 1.000000                     |
|  | Available              | 0                       |     |                              |
| Urine Leuk. Esterase (Negative) (n)                        | Negative               | 8                       | 9   | 1.000000                     |
|  | Available              | 1                       |     |                              |

\*  $p < 0.05$  is statistically significant. \*\*  $p < 0.01$  is statistically very significant. \*\*\*  $p < 0.001$  is statistically extremely signify



**Table S18.** Comparison of the short-term effect of a single dose of tocilizumab on different laboratory parameters (most recent lab results before discharge) of COVID-19 patients who received a single dose of tocilizumab (all patients vs. patients who discharged a life).

| Laboratory Characteristics                      |   |  |
|---|---|--|
| Parameter                                       | Short-term Effect of Single Dose of Tocilizumab on All Patients ( <i>n</i> = 146) | Short-term Effect of Single Dose of Tocilizumab on Patients Discharged Alive ( <i>n</i> = 133) |
| Electrolytes                                    |   |  |
| Calcium (8.6–10.0 mg/dL ) median (IQR)          | ↑N  | ↑N   |
| Phosphorus (2.5–4.5 mg/dL) median (IQR)         | ↑N  | ↑N   |
| Carbon Dioxide (22–28 mEq/L) median (IQR)       | ↑N  | ↑N   |
| Chemical Profile                                |   |  |
| Blood Urea Nitrogen (6–20 mg/dL) median (IQR)   | ↑H  | ↑N   |
| ALT (SGPT) (<50 IU/L) median (IQR)              | ↑N  | ↑N   |
| AST (SGOT) (17–59 IU/L) median (IQR)            | ↓N  | ↓N   |
| LDH (120–246 IU/L) median (IQR)                 | ↓H  | ↓H   |
| CRP, Quantitative                               |   |  |
| CRP, Quantitative (<1.0 mg/dL) median (IQR)     | ↓H  | ↓H   |
| Complete Blood Count                            |   |  |
| Hemoglobin (13.5–17.5 g/dL) median (IQR)        | –   | ↑N   |
| Hematocrit (41–53 %) median (IQR)               | –   | ↑N   |
| RDW (10.9–15.7) median (IQR)                    | ↑N  | –  |
| Platelets (150–450 K/μL) median (IQR)           | ↑N  | ↑N   |
| Mean Platelet Volume (9.0–13.0 fL) median (IQR) | –   | ↓N   |
| Neut. Absolute (1.8–7.0 K/μL) median (IQR)      | –   | ↓N   |
| Lymph. Absolute (0.9–4.9 K/μL) median (IQR)     | ↑N  | ↑N   |
| Mono. Absolute (0.0–1.0 K/μL) median (IQR)      | ↑N  | ↑N   |
| Eos. Absolute (0.0–0.4 K/μL) median (IQR)       | ↑N  | ↑N   |

**Table S19.** Baseline characteristics of COVID-19 patients who received different doses of tocilizumab categorized based on the number of doses administered to the patient.

| Parameters  |   | Total Patients      | One Dose            | Two Doses           | Three Doses         | Four Or More        | <i>p</i> -value |
|---|---|---------------------|---------------------|---------------------|---------------------|---------------------|-----------------|
| Number of patients ( <i>n</i> , %)                                    |   | 300 (100%)          | 146 (48.7%)         | 82 (27.3%)          | 36 (12.0%)          | 36 (12.0%)          |                 |
| Demographical Characteristics   |   |                     |                     |                     |                     |                     |                 |
| Age (mean ± SD)   |   | 62.00 (55.00–71.00) | 58.50 (53.00–69.00) | 65.00 (56.00–75.25) | 65.00 (59.00–72.75) | 66.50 (60.25–73.75) | 0.000485 ***    |
| Gender  | Male ( <i>n</i> , %)                      | 196 (65.3%)         | 93 (63.7%)          | 55 (67.1%)          | 24 (66.7%)          | 24 (66.7%)          | 0.952658        |
|   | Female ( <i>n</i> , %)                    | 104 (34.7%)         | 53 (36.3%)          | 27 (32.9%)          | 12 (33.3%)          | 12 (33.3%)          |                 |
| Nationality   | Saudi ( <i>n</i> , %)                     | 281 (93.7%)         | 133 (91.7%)         | 77 (93.9%)          | 35 (97.2%)          | 36 (100.0%)         | 0.290378        |
|   | Non-Saudi ( <i>n</i> , %)                 | 18 (6.0%)           | 12 (8.3%)           | 5 (6.1%)            | 1 (2.8%)            | 0 (0.0%)            |                 |
| Weight (kg) median (IQR)  |   | 83.00 (72.23–95.75) | 81.25 (73.75–96.00) | 84.65 (73.13–97.00) | 84.10 (73.50–92.38) | 81.35 (66.63–93.85) | 0.617307        |
| Body mass index (Kg/m²) median (IQR)                                  |   | 31.36 (27.43–35.76) | 31.23 (27.13–35.15) | 31.68 (27.42–36.47) | 31.55 (28.80–36.95) | 31.62 (27.73–36.54) | 0.659972        |
| Body Mass Index category  | Underweight (<18.5) ( <i>n</i> , %)       | 3 (1.0%)            | 1 (0.7%)            | 1 (1.2%)            | 1 (2.8%)            | 0 (0.0%)            | 0.889576        |
|   | Normal weight (18.5–24.9) ( <i>n</i> , %) | 27 (9.0%)           | 12 (8.2%)           | 8 (9.8%)            | 2 (5.6%)            | 5 (13.9%)           |                 |
|   | Overweight (25.0–29.9) ( <i>n</i> , %)    | 94 (31.3%)          | 48 (32.9%)          | 25 (30.5%)          | 12 (33.3%)          | 9 (25.0%)           |                 |
|   | Obese (>35.0) ( <i>n</i> , %)             | 176 (58.7%)         | 85 (58.2%)          | 48 (58.5%)          | 21 (58.3%)          | 22 (61.1%)          |                 |
| Smoking status  | Non-smoker ( <i>n</i> , %)                | 231 (78.3%)         | 111 (76.0%)         | 66 (80.5%)          | 30 (83.3%)          | 28 (77.8%)          | 0.851965        |
|   | Former-smoker ( <i>n</i> , %)             | 38 (12.9%)          | 22 (15.1%)          | 8 (9.8%)            | 3 (8.3%)            | 6 (16.7%)           |                 |
|   | Active-smoker ( <i>n</i> , %)             | 26 (8.8%)           | 13 (8.9%)           | 8 (9.8%)            | 3 (8.3%)            | 2 (5.6%)            |                 |
| Clinical Characteristics  |   |                     |                     |                     |                     |                     |                 |
| Number of Comorbidities   | 0 ( <i>n</i> , %)                         | 73 (24.3%)          | 39 (26.7%)          | 20 (24.4%)          | 8 (22.2%)           | 6 (16.7%)           | 0.254330        |
|   | 1 ( <i>n</i> , %)                         | 68 (22.7%)          | 35 (24.0%)          | 18 (22.0%)          | 10 (27.8%)          | 5 (13.9%)           |                 |
|   | 2 ( <i>n</i> , %)                         | 60 (20.0%)          | 34 (23.3%)          | 14 (17.1%)          | 6 (16.7%)           | 6 (16.7%)           |                 |
|   | 3 or more ( <i>n</i> , %)                 | 99 (33.0 %)         | 38 (26.0%)          | 30 (36.6%)          | 12 (33.3%)          | 19 (52.8%)          |                 |
| Concurrent Drug Administration  |   |                     |                     |                     |                     |                     |                 |
| Patients received at least one Antiviral drug ( <i>n</i> , %)         |   | 64 (21.3%)          | 22 (15.1%)          | 22 (26.8%)          | 9 (25.0%)           | 11 (30.6%)          | 0.071797        |
| Patient received at least one type of Corticosteroids ( <i>n</i> , %) |   | 298 (99.3)          | 144 (98.6%)         | 82 (100.0%)         | 36 (100.0%)         | 36 (100.0%)         | 0.733066        |
| Patient received Hydroxychloroquine ( <i>n</i> , %)                   |   | 63 (21%)            | 34 (23.3%)          | 20 (24.4%)          | 6 (16.7%)           | 3 (8.3%)            | 0.177919        |
| Laboratory Characteristics  |   |                     |                     |                     |                     |                     |                 |
| Electrolytes  |   |                     |                     |                     |                     |                     |                 |
| Sodium (135–145 mEq/L) (mean ± SD)                                    |   | 135.78 ± 3.94       | 135.99±3.94         | 135.78±3.91         | 135.64±4.32         | 135.08±3.73         | 0.668427        |

|   |                         |                         |                         |                         |                         |              |
|---|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|--------------|
| Potassium (3.5–5.1 mEq/L) (mean ± SD)                     | 4.36 ± 0.51             | 4.35±0.49               | 4.39±0.50               | 4.30±0.64               | 4.40±0.47               | 0.771133     |
| Calcium (8.6–10.0 mg/dL ) (mean ± SD)                     | 8.40 (8.10–8.80)        | 8.50 (8.10–8.85)        | 8.40 (8.20–8.70)        | 8.30 (7.90–8.50)        | 8.55 (7.95–8.93)        | 0.237853     |
| Magnesium (1.7–2.4 mg/dL) (mean ± SD)                     | 2.08 ±0.30              | 2.08±0.30               | 2.15±0.31               | 1.99±0.31               | 1.97±0.26               | 0.064780     |
| Phosphorus (2.5–4.5 mg/dL) median (IQR)                   | 3.50 (3.00–4.10)        | 3.40 (3.00–3.90)        | 3.50 (3.15–4.45)        | 2.90 (2.35–4.10)        | 3.80 (3.50–4.35)        | 0.161459     |
| Chloride (98–107 mEq/L) median (IQR)                      | 101.00 (98.00–103.00)   | 101.00 (98.00–104.00)   | 101.00 (97.00–103.25)   | 101.50 (99.00–103.75)   | 100.00 (97.25–102.00)   | 0.522922     |
| Carbon Dioxide (22–28 mEq/L) median (IQR)                 | 25.00 (22.00–27.00)     | 25.00 (22.00–27.00)     | 24.00 (22.00–28.00)     | 25.00 (23.00–27.75)     | 25.00 (22.00–27.00)     | 0.884520     |
| Chemical Profile  |                         |                         |                         |                         |                         |              |
| Blood Urea Nitrogen (6–20 mg/dL) median (IQR)             | 19.00 (14.00–27.00)     | 17.50 (13.00–25.25)     | 19.00 (15.00–32.00)     | 19.00 (14.00–25.75)     | 23.50 (18.00–35.25)     | 0.008393 **  |
| Creatinine (0.66–1.25 mg/dL) median (IQR)                 | 0.8000 (0.6000–1.1000)  | 0.8000 (0.6000–0.9250)  | 0.9000 (0.7000–1.2000)  | 0.8000 (0.7250–1.1000)  | 0.9000 (0.6250–1.3000)  | 0.015513 *   |
| Blood Glucose Level (73–178 mg/dL) median (IQR)           | 141.50 (111.75–210.50)  | 139.50 (108.50–209.75)  | 143.50 (111.25–194.00)  | 136.00 (116.50–200.50)  | 142.50 (120.50–240.50)  | 0.804366     |
| Lactic Acid (0.7–2.1 mmol/L) median (IQR)                 | 1.50 (1.10–2.00)        | 1.50 (1.20–2.00)        | 1.35 (1.00–1.70)        | 1.50 (1.10–2.13)        | 1.50 (1.10–2.30)        | 0.395015     |
| Cardiac Profile   |                         |                         |                         |                         |                         |              |
| Troponin High Sensitive (0.000– 0.026 ng/mL) median (IQR) | 0.0100 (0.0045–0.0285)  | 0.0070 (0.0040–0.0180)  | 0.0130 (0.0050–0.0520)  | 0.0145 (0.0040–0.0460)  | 0.0130 (.0093–0.0243)   | 0.130941     |
| B-type Natriuretic Peptide (<100 pg/mL) median (IQR)      | 59.00 (20.20–127.20)    | 49.25 (19.08–118.40)    | 69.45 (18.33–118.05)    | 26.25 (15.67–197.58)    | 103.20 (47.50–198.90)   | 0.250478     |
| Hepatic Profile   |                         |                         |                         |                         |                         |              |
| Bilirubin, Total (0.2–1.3 mg/dL) median (IQR)             | 0.5000 (0.4000–0.7000)  | 0.5000 (0.4000–0.7000)  | 0.5000 (0.4000–0.9000)  | 0.5000 (0.4000–0.8000)  | 0.5000 (0.4000–0.7000)  | 0.817465     |
| Alk. Phosphatase (53–128 IU/L) median (IQR)               | 68.00 (56.00–87.00)     | 69.00 (56.00–89.00)     | 67.00 (54.50–81.50)     | 67.50 (55.50–82.50)     | 68.00 (54.50–101.25)    | 0.455784     |
| ALT (SGPT) (<50 IU/L) median (IQR)                        | 31.00 (21.00–48.00)     | 32.00 (22.00–49.50)     | 31.00 (19.00–49.00)     | 32.00 (22.75–48.25)     | 29.00 (22.00–40.25)     | 0.777216     |
| AST (SGOT) (17–59 IU/L) median (IQR)                      | 44.50 (35.00–62.50)     | 43.00 (34.50–59.00)     | 46.00 (36.00–71.50)     | 45.00 (39.75–80.75)     | 43.00 (33.50–69.75)     | 0.561416     |
| LDH (120–246 IU/L) median (IQR)                           | 356.50 (280.00–462.00)  | 325.00 (262.00–415.25)  | 387.50 (311.25–493.50)  | 428.50 (326.75–648.75)  | 379.50 (299.75–612.50)  | 0.000539 *** |
| Iron/Anemia Profile                                       |                         |                         |                         |                         |                         |              |
| Ferritin (21.81–274.66 ng/mL) median (IQR)                | 786.00 (421.00–1538.00) | 735.00 (406.75–1415.78) | 844.00 (504.00–1634.50) | 516.50 (211.75–1158.50) | 973.50 (420.25–1610.50) | 0.446257     |
| CRP, Quantitative   |                         |                         |                         |                         |                         |              |
| CRP, Quantitative (<1.0 mg/dL) median (IQR)               | 15.60 (6.30–20.40)      | 13.90 (5.75–20.00)      | 17.10 (6.60–21.20)      | 17.90 (7.00–22.40)      | 16.50 (6.30–20.40)      | 0.140567     |
| Complete Blood Count                                      |                         |                         |                         |                         |                         |              |
| WBC (4.0–10.0 K/ $\mu$ L) median (IQR)                    | 7.45 (5.30–10.10)       | 7.40 (5.40–10.13)       | 7.70 (4.78–10.18)       | 9.10 (5.80–12.15)       | 6.05 (4.50–8.95)        | 0.073328     |
| RBC (4.5–5.9 M/ $\mu$ L) median (IQR)                     | 4.61 (4.15–5.11)        | 4.74 (4.25–5.23)        | 4.50 (4.09–5.00)        | 4.59 (4.19–4.92)        | 4.47 (4.11–5.11)        | 0.102481     |
| Hemoglobin (13.5–17.5 g/dL) (mean ± SD)                   | 12.31 ±1.89             | 12.29±1.80              | 12.26±2.00              | 12.32±1.92              | 12.50±2.01              | 0.932202     |
| Hematocrit (41–53 %) (mean ± SD)                          | 38.05 ±5.34             | 38.12±4.94              | 37.85±5.97              | 37.84±5.52              | 38.47±5.42              | 0.935646     |

|  |                        |                        |                         |                        |                        |              |
|--|------------------------|------------------------|-------------------------|------------------------|------------------------|--------------|
| MCV (77–96 fL) median (IQR)                              | 84.00 (77.30–88.38)    | 82.60 (73.88–87.70)    | 85.10 (80.48–89.18)     | 82.45 (78.83–87.20)    | 86.25 (82.10–88.55)    | 0.008551 **  |
| MCH (26–34 pg) median (IQR)                              | 27.30 (24.80–29.18)    | 26.90 (22.98–29.10)    | 27.60 (26.05–29.40)     | 27.40 (25.20–28.35)    | 28.40 (25.33–29.75)    | 0.041851 *   |
| MCHC (32–36 g/dL) (mean ± SD)                            | 32.32 ±1.58            | 32.21±1.67             | 32.40±1.55              | 32.48±1.22             | 32.41±1.56             | 0.705016     |
| RDW (10.9–15.7) median (IQR)                             | 13.75 (2.90–14.80)     | 13.80 (12.78–15.33)    | 13.85 (13.00–14.80)     | 13.60 (12.90–14.63)    | 13.45 (12.83–14.88)    | 0.714308     |
| Platelets (150–450 K/μL) median (IQR)                    | 233.00 (183.00–297.75) | 245.00 (196.75–321.00) | 225.50 ((178.50–290.25) | 240.00 (186.75–265.00) | 177.00 (144.50–249.50) | 0.000858 *** |
| Mean Platelet Volume (9.0–13.0 fL) median (IQR)          | 10.60 (10.00–11.30)    | 10.60 (9.73–11.38)     | 10.50 (10.10–11.08)     | 10.80 (10.35–11.30)    | 11.00 (10.23–11.58)    | 0.206676     |
| Platelets Distribution Width (10.1–16.1 fL) median (IQR) | 12.30 (11.20–14.10)    | 12.30 (11.10–14.43)    | 12.10 (11.20–13.48)     | 12.60 (11.60–13.73)    | 12.80 (11.45–15.38)    | 0.309775     |
| Neut. Absolute (1.8–7.0 K/μL) median (IQR)               | 6.05 (3.80–8.50)       | 5.95 (3.90–8.27)       | 6.10 (3.63–8.55)        | 7.35 (4.30–9.60)       | 4.65 (2.85–7.33)       | 0.095240     |
| Lymph. Absolute (0.9–4.9 K/μL) median (IQR)              | 0.8000 (0.6000–1.1000) | 0.8000 (0.6000–1.2000) | 0.7000 (0.5000–1.0000)  | 0.8000 (0.6000–1.0000) | 0.8000 (0.5250–0.9750) | 0.042841 *   |
| Mono. Absolute (0.0–1.0 K/μL) median (IQR)               | 0.3000 (0.2000–0.5000) | 0.3000 (0.2000–0.5000) | 0.4000 (0.2000–0.6000)  | 0.3000 (0.2000–0.6750) | 0.3000 (0.2000–0.5000) | 0.409104     |
| Eos. Absolute (0.0–0.4 K/μL) median (IQR)                | 0.0000 (.0000–0.0000)  | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000) | 0.241188     |
| Baso. Absolute (0.0–0.1 K/μL) median (IQR)               | 0.0000 (.0000–0.0000)  | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000)  | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000) | 0.287612     |
| Band Neutrophil Absolute (0.0–0.5 K/μL) median (IQR)     | 0.2700 (0.1300–0.5900) | 0.3050 (0.1225–0.6050) | 0.2500 (0.1300–0.5650)  | 0.7500 (0.2300–1.4150) | 0.1800 (0.1250–0.3000) | 0.111886     |
| Coagulation  |                        |                        |                         |                        |                        |              |
| Prothrombin Time (9.8–12.7 Secs) median (IQR)            | 11.30 (10.80–11.90)    | 11.40 (10.73–11.90)    | 11.25 (10.90–11.98)     | 10.90 (10.30–11.80)    | 11.30 (10.65–11.70)    | 0.747834     |
| I.N. Ratio (1.0–1.2 Ratio) median (IQR)                  | 1.00 (1.00–1.10)       | 1.00 (1.00–1.10)       | 1.00 (1.00–1.10)        | 1.00 (1.00–1.10)       | 1.00 (1.00–1.10)       | 0.868973     |
| APTT (22–33 Secs) median (IQR)                           | 30.00 (28.00–33.00)    | 29.50 (27.25–34.50)    | 31.00 (28.00–33.00)     | 28.00 (28.00–32.50)    | 29.50 (28.00–32.25)    | 0.833412     |
| D-Dimer Quantitative (0.0–0.7 mg/L FEU) median (IQR)     | 0.73 (0.43–1.41)       | 0.66 (0.37–1.33)       | 0.83 (0.44–1.72)        | 0.76 (0.46–1.36)       | 0.90 (0.51–1.21)       | 0.291413     |
| Urine Analysis   |                        |                        |                         |                        |                        |              |
| Urine Specific Gravity (1.000–1.030) (mean ± SD)         | 1.0197±.00901          | 1.0200±.00867          | 1.0197±.00989           | 1.0174±.00806          | 1.0206±.00951          | 0.585585     |
| Urine pH (4.5–8.0)                                       | 5 (n, %)               | 72 (24.0%)             | 38 (39.2%)              | 18 (34.6%)             | 10 (41.7%)             | 6 (27.3%)    |
|  | 5.5 (n, %)             | 62 (20.7%)             | 29 (29.9%)              | 14 (26.9%)             | 9 (37.5%)              | 10 (45.5%)   |
|  | 6 (n, %)               | 28 (9.3%)              | 12 (12.4%)              | 11 (21.2%)             | 2 (8.3%)               | 3 (13.6%)    |
|  | 6.5 (n, %)             | 14 (4.7%)              | 9 (9.3%)                | 3 (5.8%)               | 1 (4.2%)               | 1 (4.5%)     |
|  | 7 (n, %)               | 15 (5.0%)              | 7 (7.2%)                | 5 (9.6%)               | 2 (8.3%)               | 1 (4.5%)     |
|  | 7.5 (n, %)             | 4 (1.3%)               | 2 (2.1%)                | 1 (1.9%)               | 0 (0.0%)               | 1 (4.5%)     |
| Urine Protein (Negative) (n, %)                          | Negative               | 92 (30.7%)             | 46 (47.4%)              | 25 (48.1%)             | 12 (50.0%)             | 9 (40.9%)    |
|  | Available              | 103 (34.3%)            | 51 (52.6%)              | 27 (51.9%)             | 12 (50.0%)             | 13 (59.1%)   |
|  | Negative               | 138 (46.0%)            | 74 (76.3%)              | 29 (55.8%)             | 20 (83.3%)             | 15 (68.2%)   |

0.925127

0.931261

0.029464 \*

|  |           |             |            |             |             |             |             |
|--|-----------|-------------|------------|-------------|-------------|-------------|-------------|
| Urine Glucose (Negative)<br>(n, %)           | Available | 57 (19.0%)  | 23 (23.7%) | 23 (44.2%)  | 4 (16.7%)   | 7 (31.8%)   |             |
| Urine Ketone (Negative)<br>(n, %)            | Negative  | 125 (41.7%) | 59 (60.8%) | 32 (61.5%)  | 18 (75.0%)  | 16 (72.7%)  | 0.466107    |
|  | Available | 70 (23.3%)  | 38 (39.2%) | 20 (38.5%)  | 6 (25.0%)   | 6 (27.3%)   |             |
| Urine Blood (Negative)<br>(n, %)             | Negative  | 105 (35.0%) | 49 (50.5%) | 32 (61.5%)  | 13 (54.2%)  | 11 (50.0%)  | 0.683917    |
|  | Trace     | 46 (15.3%)  | 25 (25.8%) | 11 (21.2%)  | 4 (16.7%)   | 6 (27.3%)   |             |
|  | Moderate  | 36 (12.0%)  | 18 (18.6%) | 6 (11.5%)   | 7 (29.2%)   | 5 (22.7%)   |             |
|  | Numerous  | 8 (2.7%)    | 5 (5.2%)   | 3 (5.8%)    | 0 (0.0%)    | 0 (0.0%)    |             |
| Urine Bilirubin (Negative)<br>(n, %)         | Negative  | 193 (64.3%) | 96 (99.0%) | 52 (100.0%) | 23 (95.8%)  | 22 (100.0%) | 0.487179    |
|  | Available | 2 (.7%)     | 1 (1.0%)   | 0 (0.0%)    | 1 (4.2%)    | 0 (0.0%)    |             |
| Urine Urobilinogen (0.0–1.0<br>EU/dL) (n, %) | Normal    | 166 (55.3%) | 79 (81.4%) | 48 (92.3%)  | 17 (70.8%)  | 22 (100.0%) | 0.008260 ** |
|  | Abnormal  | 29 (9.7%)   | 18 (18.6%) | 4 (7.7%)    | 7 (29.2%)   | 0 (0.0%)    |             |
| Urine Nitrites (Negative)<br>(n, %)          | Negative  | 193 (64.3%) | 96 (99.0%) | 52 (100.0%) | 24 (100.0%) | 21 (95.5%)  | 0.364103    |
|  | Available | 2 (.7%)     | 1 (1.0%)   | 0 (0.0%)    | 0 (0.0%)    | 1 (4.5%)    |             |
| Urine Leuk. Esterase (Nega-<br>tive) (n, %)  | Negative  | 182 (60.7%) | 89 (91.8%) | 50 (96.2%)  | 24 (100.0%) | 19 (86.4%)  | 0.205746    |
|  | Available | 13 (4.3%)   | 8 (8.2%)   | 2 (3.8%)    | 0 (0.0%)    | 3 (13.6%)   |             |

\*  $p < 0.05$  is statistically significant; \*\*  $p < 0.01$  is statistically very significant; \*\*\*  $p < 0.001$  is statistically extremely significant.

**Table S20.** Kaplan–Meir survival analysis (days) post last dose of tocilizumab among different dose groups of COVID–19 patients.

| Number of Tocilizumab Doses | 28 Days Mean Survival Time (days) After the Last Dose of Tocilizumab (mean ± Std. Error) | 95% Confidence Interval | <i>p</i> -value | 90 Days Mean Survival Time (days) After the Last Dose of Tocilizumab (mean ± Std. Error) | 95% Confidence Interval | <i>p</i> -value |
|-----------------------------|--|-------------------------|-----------------|--|-------------------------|-----------------|
| One dose                    | 8.77±1.35  | (6.11–11.42)            | 0.750664        | 12.87±3.09   | (6.81–18.93)            | 0.318854        |
| Two doses                   | 9.75±1.31  | (7.18–12.32)            |                 | 10.60±1.52   | (7.62–13.58)            |                 |
| Three doses                 | 7.17±2.88  | (1.52–12.81)            |                 | 11.71±5.16   | (1.60–21.82)            |                 |
| Four or more doses          | 7.17±2.88  | (5.11–10.73)            |                 | 18.47±4.52   | (9.62–27.32)            |                 |
| Total patients              | 8.82±0.78  | (7.30–10.34)            |                 | 13.34±1.63   | (10.15–16.54)           |                 |



|   |          |                        |                        |                        |                        |                        |              |
|---|----------|------------------------|------------------------|------------------------|------------------------|------------------------|--------------|
| CRP, Quantitative (<1.0 mg/dL) (mean ± SD)              | 227      | 0.80 (0.49–1.90)       | 1.40 (0.60–2.50)       | 0.60 (0.49–1.05)       | 0.49 (0.49–1.40)       | 0.49 (0.49–0.70)       | 0.000001 *** |
| Complete Blood Count                                    |          |                        |                        |                        |                        |                        |              |
| WBC (4.0–10.0 K/μL) (mean ± SD)                         | 234      | 7.98±3.43              | 7.85±3.52              | 8.26±3.12              | 8.65±3.35              | 6.95±3.79              | 0.354469     |
| RBC (4.5–5.9 M/μL) (mean ± SD)                          | 234      | 4.73±.77               | 4.82±0.73              | 4.68±0.88              | 4.72±0.63              | 4.28±0.80              | 0.039838 *   |
| Hemoglobin (13.5–17.5 g/dL) (mean ± SD)                 | 234      | 12.55±1.84             | 12.52±1.87             | 12.68±2.03             | 12.80±1.47             | 11.97±1.54             | 0.457129     |
| Hematocrit (41–53 %) (mean ± SD)                        | 234      | 38.93±5.00             | 38.87±4.93             | 39.28±5.70             | 39.83±3.89             | 36.86±4.58             | 0.230721     |
| MCV (77–96 fL) (mean ± SD)                              | 234      | 83.14±8.35             | 81.43±8.65             | 84.86±7.68             | 85.01±6.27             | 87.31±8.41             | 0.002726 **  |
| MCH (26–34 pg) (mean ± SD)                              | 234      | 26.83±3.46             | 26.27±3.76             | 27.38±3.03             | 27.32±2.54             | 28.36±3.02             | 0.028848*    |
| MCHC (32–36 g/dL) (mean ± SD)                           | 234      | 32.18±1.61             | 32.13±1.78             | 32.24±1.41             | 32.10±1.26             | 32.47±1.37             | 0.775783     |
| RDW (10.9–15.7) (mean ± SD)                             | 234      | 13.80 (13.00–15.83)    | 13.70 (12.80–15.70)    | 13.75 (13.10–15.67)    | 13.80 (13.00–14.95)    | 15.40 (14.60–16.45)    | 0.043671 *   |
| Platelets (150–450 K/μL) (mean ± SD)                    | 234      | 305.88±116.92          | 323.81±114.88          | 286.84±112.34          | 317.69±124.60          | 215.67±86.64           | 0.001161 **  |
| Mean Platelet Volume (9.0–13.0 fL) (mean ± SD)          | 220      | 10.40 (9.83–11.10)     | 10.40 (9.70–11.10)     | 10.45 (9.98–11.00)     | 10.50 (9.80–11.00)     | 11.40 (10.10–11.95)    | 0.208165     |
| Platelets Distribution Width (10.1–16.1 fL) (mean ± SD) | 220      | 12.10 (10.80–13.88)    | 12.05 (10.60–13.90)    | 12.10 (11.25–13.08)    | 12.10 (10.70–13.60)    | 13.90 (10.85–15.45)    | 0.494551     |
| Neut. Absolute (1.8–7.0 K/μL) (mean ± SD)               | 230      | 5.05 (3.10–7.50)       | 5.00 (3.10–7.10)       | 5.35 (3.10–8.28)       | 5.20 (3.45–8.30)       | 4.25 (2.03–6.00)       | 0.365829     |
| Lymph. Absolute (0.9–4.9 K/μL) (mean ± SD)              | 230      | 1.63±.86               | 1.54±0.87              | 1.65±0.81              | 1.91±0.97              | 1.73±0.75              | 0.192007     |
| Mono. Absolute (0.0–1.0 K/μL) (mean ± SD)               | 230      | 0.6000 (0.4000–0.8000) | 0.5000 (0.4000–0.8000) | 0.7000 (0.4000–0.8000) | 0.6000 (0.4500–0.8000) | 0.6000 (0.4000–0.8250) | 0.677961     |
| Eos. Absolute (0.0–0.4 K/μL) (mean ± SD)                | 230      | 0.1000 (0.0000–0.2000) | 0.0000 (0.0000–0.1000) | 0.1000 (0.0000–0.2000) | 0.0000 (0.0000–0.2000) | 0.1000 (0.0000–0.2000) | 0.008098 **  |
| Baso. Absolute (0.0–0.1 K/μL) (mean ± SD)               | 230      | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.0000) | 0.0000 (0.0000–0.1000) | 0.0000 (0.0000–0.0500) | 0.0000 (0.0000–0.0250) | 0.061805     |
| Band Neutrophil Absolute (0.0–0.5 K/μL) (mean ± SD)     | 77       | 0.2600 (0.1400–0.5450) | 0.2300 (0.1300–0.4625) | 0.3400 (0.1275–0.5575) | 0.6950 (0.5175–1.0325) | 0.2200 (0.1200–0.5850) | 0.041337 *   |
| Coagulation   |          |                        |                        |                        |                        |                        |              |
| Prothrombin Time (9.8–12.7 Secs) (mean ± SD)            | 81       | 11.70 (11.00–12.35)    | 11.80 (11.18–12.63)    | 11.65 (11.00–12.53)    | 11.55 (10.90–12.20)    | 11.80 (11.40–12.40)    | 0.797284     |
| I.N. Ratio (1.0–1.2 Ratio) (mean ± SD)                  | 81       | 1.10 (1.00–1.10)       | 1.10 (1.00–1.10)       | 1.10 (1.00–1.13)       | 1.00 (1.00–1.10)       | 1.10 (1.00–1.10)       | 0.700831     |
| APTT (22–33 Secs) (mean ± SD)                           | 77       | 26.88±8.06             | 27.04±2.94             | 29.35±14.10            | 25.07±1.33             | 24.67±2.29             | 0.257836     |
| D-Dimer Quantitative (0.0–0.7 mg/L FEU) (mean ± SD)     | 188      | 0.81 (0.42–1.49)       | 0.79 (0.40–1.40)       | 0.63 (0.39–1.22)       | 1.13 (0.46–4.03)       | 1.32 (0.46–2.36)       | 0.118139     |
| Urine Analysis  |          |                        |                        |                        |                        |                        |              |
| Urine Specific Gravity (1.000–1.030) (mean ± SD)        | 37       | 1.01959±.00971         | 1.02319±0.00974        | 1.01763±0.00850        | 1.01175±0.00544        | 1.01250±0.00714        | 0.039138 *   |
| Urine pH (4.5–8.0)                                      | 5 (n, %) | 7 (3.0%)               | 5 (23.8%)              | 1 (12.5%)              | 1 (25.0%)              | 0 (0.0%)               | 0.646419     |



|                            |            |    |            |             |           |            |            |          |
|----------------------------|------------|----|------------|-------------|-----------|------------|------------|----------|
|                            | 5.5 (n, %) |    | 7 (3.0%)   | 5 (23.8%)   | 1 (12.5%) | 0 (0.0%)   | 1 (25.0%)  |          |
|                            | 6 (n, %)   |    | 7 (3.0%)   | 4 (19.0%)   | 2 (25.0%) | 0 (0.0%)   | 1 (25.0%)  |          |
|                            | 6.5 (n, %) |    | 11 (4.6%)  | 4 (19.0%)   | 4 (50.0%) | 1 (25.0%)  | 2 (50.0%)  |          |
|                            | 7 (n, %)   |    | 5 (2.1%)   | 3 (14.3%)   | 0 (0.0%)  | 2 (50.0%)  | 0 (0.0%)   |          |
|                            | 7.5 (n, %) |    | 0 (0.0%)   | 0 (0.0%)    | 0 (0.0%)  | 0 (0.0%)   | 0 (0.0%)   |          |
| Urine Protein (Negative)   | Negative   | 37 | 21 (8.9%)  | 13 (61.9%)  | 4 (50.0%) | 2 (50.0%)  | 2 (80.0%)  | 0.953978 |
| (n, %)                     | Available  |    | 16 (6.8%)  | 8 (38.1%)   | 4 (50.0%) | 2 (50.0%)  | 2 (50.0%)  |          |
| Urine Glucose (Negative)   | Negative   | 37 | 29 (12.2%) | 16 (76.2%)  | 7 (87.5%) | 3 (75.0%)  | 3 (75.0%)  | 0.930551 |
| (n, %)                     | Available  |    | 8 (3.4%)   | 5 (23.8%)   | 1 (12.5%) | 1 (25.0%)  | 1 (25.0%)  |          |
| Urine Ketone (Negative)    | Negative   | 37 | 29 (12.2%) | 16 (76.2%)  | 7 (87.5%) | 4 (100.0%) | 2 (50.0%)  | 0.374272 |
| (n, %)                     | Available  |    | 8 (3.4%)   | 5 (23.8%)   | 1 (12.5%) | 0 (0.0%)   | 2 (50.0%)  |          |
| Urine Blood (Negative)     | Negative   | 37 | 15 (6.3%)  | 8 (38.1%)   | 4 (50.0%) | 1 (25.0%)  | 2 (50.0%)  | 0.981251 |
| (n, %)                     | Trace      |    | 7 (3.0%)   | 5 (23.8%)   | 1 (12.5%) | 1 (25.0%)  | 0 (0.0%)   |          |
|                            | Moderate   |    | 8 (3.4%)   | 5 (23.8%)   | 1 (12.5%) | 1 (25.0%)  | 1 (25.0%)  |          |
|                            | Numerous   |    | 7 (3.0%)   | 3 (14.3%)   | 2 (25.0%) | 1 (25.0%)  | 1 (25.0%)  |          |
| Urine Bilirubin (Negative) | Negative   | 37 | 36 (15.2%) | 21 (100%)   | 7 (87.5%) | 4 (100.0%) | 4 (100.0%) | 0.432432 |
| (n, %)                     | Available  |    | 1 (.4%)    | 0 (0.0%)    | 1 (12.5%) | 0 (0.0%)   | 0 (0.0%)   |          |
| Urine Urobilinogen         | Normal     | 37 | 32 (13.5%) | 17 (81.0%)  | 7 (87.5%) | 4 (100.0%) | 4 (100.0%) | 1.000000 |
| (0.0–1.0 EU/dL) (n, %)     | Abnormal   |    | 5 (2.1%)   | 4 (19.0%)   | 1 (12.5%) | 0 (0.0%)   | 0 (0.0%)   |          |
| Urine Nitrites (Negative)  | Negative   | 37 | 34 (14.3%) | 21 (100.0%) | 6 (75.0%) | 4 (100.0%) | 3 (75.0%)  | 0.055598 |
| (n, %)                     | Available  |    | 3 (1.3%)   | 0 (0.0%)    | 2 (25.0%) | 0 (0.0%)   | 1 (25.0%)  |          |
| Urine Leuk. Esterase       | Negative   | 37 | 29 (12.2%) | 18 (85.7%)  | 5 (62.5%) | 4 (100.0%) | 2 (50.0%)  | 0.181398 |
| (Negative) (n, %)          | Available  |    | 8 (3.4%)   | 3 (14.3%)   | 3 (37.5%) | 0 (0.0%)   | 2 (50.0%)  |          |

\*  $p < 0.05$  is statistically significant; \*\*  $p < 0.01$  is statistically very significant; \*\*\*  $p < 0.001$  is statistically extremely significant; <sup>i</sup> The most recent lab results before discharge/decease and after the first dose of Tocilizumab for patients received one dose of tocilizumab; <sup>ii</sup> The most recent lab results before discharge/decease and after the second dose of Tocilizumab for patients received two doses of tocilizumab; <sup>iii</sup> The most recent lab results before discharge/decease and after the third dose of Tocilizumab for patients received three doses of tocilizumab; <sup>iv</sup> The most recent lab results before discharge/decease and after the fourth dose of Tocilizumab for patients received four doses and more of tocilizumab.

**Table S22.** Number of patients who had an infection before and after tocilizumab administrations and the number of incidences.

|       | Before Tocilizumab |                      | After Tocilizumab  |                      |
|-------|--------------------|----------------------|--------------------|----------------------|
|       | Number of Patients | Number of Incidences | Number of Patients | Number of Incidences |
| 0     | 278                | 0                    | 237                | 0                    |
| 1     | 21                 | 21                   | 34                 | 34                   |
| 2     | 1                  | 2                    | 16                 | 32                   |
| 3     | 0                  | 0                    | 6                  | 18                   |
| 4     | 0                  | 0                    | 4                  | 16                   |
| 5     | 0                  | 0                    | 2                  | 10                   |
| 6     | 0                  | 0                    | 1                  | 6                    |
| Total | 22/300             | 23                   | 63/300             | 116                  |

**Table S23.** Number of incidences of infection before and after tocilizumab administrations based on their anatomical locations.

| Anatomical Location of the Infection | Number of Incidences Before Tocilizumab | Number of Incidences After Starting Tocilizumab | Test      | <i>p</i> -value             |
|--------------------------------------|---|---|-----------|-----------------------------|
| Blood                                | 3                                       | 22  | Sign test | 0.007538 **                 |
| Respiratory                          | 14                                      | 57  |           | 0.000004 ***                |
| Urine                                | 6                                       | 37  |           | 0.000048 ***                |
| Total                                | 23                                      | 116   |           | $5.7734 \times 10^{-7}$ *** |

\*  $p < 0.05$  is statistically significant; \*\*  $p < 0.01$  is statistically very significant; \*\*\*  $p < 0.001$  is statistically extremely significant.

**Table S24.** Types of microorganisms before and after tocilizumab based on their types.

| Microorganism Type  | Number of Incidences Before Tocilizumab | Number of Incidences After Tocilizumab |
|---------------------|---|--|
| Bacterial infection | 14                                      | 55                                     |
| Fungal infection    | 9                                       | 61                                     |
| Total               | 23                                      | 116                                    |

**Table S25.** Detailed microorganisms before and after tocilizumab.

| Microorganism Name                            | Number of Incidences Before Tocilizumab | Number Of Incidences After Tocilizumab |
|---|---|--|
| <i>Acinetobacter baumannii</i> complex        |   | 2                                      |
| <i>Aspergillus niger</i>                      |   | 1                                      |
| <i>Aspergillus</i> species                    |   | 4                                      |
| <i>Burkholderia cepacia</i> group             |   | 2                                      |
| <i>Candida albicans</i>                       | 4                                       | 33                                     |
| <i>Candida dubliniensis</i>                   | 2                                       | 5                                      |
| <i>Candida glabrata</i>                       | 1                                       |  |
| <i>Candida kefyr</i>                          |   | 1                                      |
| <i>Candida krusei</i>                         |   | 2                                      |
| <i>Candida lusitanae</i>                      |   | 2                                      |
| <i>Candida parapsilosis</i>                   |   | 3                                      |
| <i>Candida tropicalis</i>                     | 2                                       | 8                                      |
| <i>Cryptococcus laurentii</i>                 |   | 1                                      |
| <i>Enterobacter cloacae</i>                   |   | 1                                      |
| <i>Enterococcus faecalis</i>                  | 1                                       | 3                                      |
| <i>Escherichia coli</i>                       | 3                                       | 6                                      |
| <i>Escherichia coli</i> ESBL producing strain |   | 4                                      |
| <i>Haemophilus parainfluenzae</i>             |   | 1                                      |
| <i>Klebsiella pneumoniae</i>                  | 2                                       | 5                                      |
| MRSA  | 4                                       | 7                                      |
| <i>Pseudomonas aeruginosa</i>                 | 2                                       | 5                                      |
| <i>Serratia marcescens</i>                    |   | 1                                      |
| <i>Staphylococcus aureus</i>                  | 1                                       | 3                                      |
| <i>Staphylococcus epidermidis</i>             | 1                                       | 9                                      |
| <i>Staphylococcus haemolyticus</i>            |   | 1                                      |
| <i>Stenotrophomonas maltophilia</i>           |   | 5                                      |
| Yeast   |   | 1                                      |
| Total   | 23                                      | 116                                    |

**Table S26.** Detailed microorganisms before and after tocilizumab administration based on their anatomical location.

| Anatomical Location | Microorganism Name                            | Number of Incidences Before Tocilizumab | Number of Incidences After Tocilizumab |
|---------------------|---|---|--|
| Blood               | <i>Acinetobacter baumannii</i> complex        | –                                       | 1                                      |
|                     | <i>Burkholderia cepacia</i> group             | –                                       | 1                                      |
|                     | <i>Candida albicans</i>                       | –                                       | 3                                      |
|                     | <i>Candida tropicalis</i>                     | –                                       | 1                                      |
|                     | <i>Enterococcus faecalis</i>                  | –                                       | 2                                      |
|                     | <i>Klebsiella pneumoniae</i>                  | –                                       | 1                                      |
|                     | MRSA  | –                                       | 2                                      |
|                     | <i>Serratia marcescens</i>                    | –                                       | 1                                      |
|                     | <i>Staphylococcus aureus</i>                  | 1                                       | 1                                      |
|                     | <i>Staphylococcus haemolyticus</i>            | –                                       | 1                                      |
|                     | <i>Staphylococcus epidermidis</i>             | 1                                       | 6                                      |
|                     | <i>Stenotrophomonas maltophilia</i>           | –                                       | 1                                      |
|                     | <i>Pseudomonas aeruginosa</i>                 | 1                                       | 1                                      |
| Respiratory         | <i>Acinetobacter baumannii</i> complex        | –                                       | 1                                      |
|                     | <i>Aspergillus niger</i>                      | –                                       | 1                                      |
|                     | <i>Aspergillus species</i>                    | –                                       | 4                                      |
|                     | <i>Burkholderia cepacia</i> group             | –                                       | 1                                      |
|                     | <i>Candida albicans</i>                       | 4                                       | 16                                     |
|                     | <i>Candida dubliniensis</i>                   | 2                                       | 3                                      |
|                     | <i>Candida glabrata</i>                       | 1                                       |  |
|                     | <i>Candida krusei</i>                         | –                                       | 1                                      |
|                     | <i>Candida lusitaniae</i>                     | –                                       | 1                                      |
|                     | <i>Candida parapsilosis</i>                   | –                                       | 2                                      |
|                     | <i>Candida tropicalis</i>                     | 1                                       | 3                                      |
|                     | <i>Cryptococcus laurentii</i>                 | –                                       | 1                                      |
|                     | <i>Enterobacter cloacae</i>                   | –                                       | 1                                      |
|                     | <i>Escherichia coli</i>                       | –                                       | 2                                      |
|                     | <i>Haemophilus parainfluenzae</i>             | –                                       | 1                                      |
|                     | <i>Klebsiella pneumoniae</i>                  | 1                                       | 2                                      |
|                     | MRSA  | 4                                       | 5                                      |
|                     | <i>Pseudomonas aeruginosa</i>                 | 1                                       | 2                                      |
|                     | <i>Staphylococcus Aureus</i>                  | –                                       | 2                                      |
|                     | <i>Staphylococcus epidermidis</i>             | –                                       | 3                                      |
|                     | <i>Stenotrophomonas maltophilia</i>           | –                                       | 4                                      |
|                     | Yeast   | –                                       | 1                                      |
| Urine               | <i>Candida albicans</i>                       | –                                       | 14                                     |
|                     | <i>Candida dubliniensis</i>                   | –                                       | 2                                      |
|                     | <i>Candida kefyr</i>                          | –                                       | 1                                      |
|                     | <i>Candida krusei</i>                         | –                                       | 1                                      |
|                     | <i>Candida lusitaniae</i>                     | –                                       | 1                                      |
|                     | <i>Candida parapsilosis</i>                   | –                                       | 1                                      |
|                     | <i>Candida tropicalis</i>                     | 1                                       | 4                                      |
|                     | <i>Enterococcus faecalis</i>                  | 1                                       | 1                                      |
|                     | <i>Escherichia coli</i>                       | 3                                       | 4                                      |
|                     | <i>Escherichia coli</i> ESBL producing strain | –                                       | 4                                      |
|                     | <i>Klebsiella pneumoniae</i>                  | 1                                       | 2                                      |
|                     | <i>Pseudomonas aeruginosa</i>                 | –                                       | 2                                      |

## References

- Al BahraniS.Y.; Al-TawfiqJ.A.; AlshaerA.R.; ShilashA.; AlswefyK.; Al-ZayerR.S.; AbouelelaA.M. A Case Series of Severe Hospitalized COVID-19 Patients Treated with Tocilizumab and Glucocorticoids: A Report from Saudi Arabian Hospital. *J. Epidemiology Glob. Heal.* **2021**, *11*, 233–237, doi:10.2991/jegh.k.210112.001.
- Assiri, A., et al., COVID-19 related treatment and outcomes among COVID-19 ICU patients: A retrospective cohort study. *J Infect Public Health*, 2021. 14(9): p. 1274–1278.
- StoneJ.H.; FrigaultM.J.; Serling-BoydN.J.; FernandesA.D.; HarveyL.; FoulkesA.S.; HorickN.K.; HealyB.C.; ShahR.; BensaciA.M.; et al. Efficacy of Tocilizumab in Patients Hospitalized with Covid-19. *New Engl. J. Med.* **2020**, *383*, 2333–2344, doi:10.1056/nejmoa2028836.
- Al-BaadaniA.; EltayebN.; AlsufyaniE.; AlbahraniS.; BashariS.; AlbayathH.; BatubaraE.; BalloolS.; Al AssiriA.; FaqihF.; et al. Efficacy of tocilizumab in patients with severe COVID-19: Survival and clinical outcomes. *J. Infect. Public Heal.* **2021**, *14*, 1021–1027, doi:10.1016/j.jiph.2021.05.015.
- VeigaV.C.; PratsJ.A.G.G.; FariasD.L.C.; RosaR.G.; DouradoL.K.; ZampieriF.G.; MachadoF.R.; LopesR.D.; BerwangerO.; AzevedoL.C.P.; et al. Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial. *BMJ* **2021**, *372*, n84, doi:10.1136/bmj.n84.
- Salvarani, C., et al., Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 Pneumonia: A Randomized Clinical Trial. *JAMA Intern Med*, 2021. 181(1): p. 24–31.
- CapraR.; De RossiN.; MattioliF.; RomanelliG.; ScarpazzaC.; SormaniM.P.; CossiS. Impact of low dose tocilizumab on mortality rate in patients with COVID-19 related pneumonia. *Eur. J. Intern. Med.* **2020**, *76*, 31–35, doi:10.1016/j.ejim.2020.05.009.
- Wadud, N., et al., IMPROVED SURVIVAL OUTCOME IN PATIENTS WITH SARS-COV-2 (COVID-19) ARDS WITH TOCILIZUMAB ADMINISTRATION. *Chest*, 2020. 158(4): p. A696–A697.
- Roumier, M., et al., Interleukin-6 blockade for severe COVID-19. *medRxiv*, 2020: p. 2020.04.20.20061861.
- Ramaswamy, M., et al., Off-Label Real World Experience Using Tocilizumab for Patients Hospitalized with COVID-19 Disease in a Regional Community Health System: A Case-Control Study. *medRxiv*, 2020: p. 2020.05.14.20099234.
- Morena, V.; Milazzo, L.; Oreni, L.; Bestetti, G.; Fossali, T.; Bassoli, C.; Torre, A.; Cossu, M.V.; Minari, C.; Ballone, E.; et al. Off-label use of tocilizumab for the treatment of SARS-CoV-2 pneumonia in Milan, Italy. *Eur. J. Intern. Med.* **2020**, *76*, 36–42, doi:10.1016/j.ejim.2020.05.011.
- Quartuccio, L.; Sonaglia, A.; McGonagle, D.; Fabris, M.; Peghin, M.; Pecori, D.; De Monte, A.; Bove, T.; Curcio, F.; Bassi, F.; et al. Profiling COVID-19 pneumonia progressing into the cytokine storm syndrome: Results from a single Italian Centre study on tocilizumab versus standard of care. *J. Clin. Virol.* **2020**, *129*, 104444, doi:10.1016/j.jcv.2020.104444.
- Biran, N.; Ip, A.; Ahn, J.; Go, R.C.; Wang, S.; Mathura, S.; A Sinclair, B.; Bednarz, U.; Marafelias, M.; Hansen, E.; et al. Tocilizumab among patients with COVID-19 in the intensive care unit: a multicentre observational study. *Lancet Rheumatol.* **2020**, *2*, e603–e612, doi:10.1016/s2665-9913(20)30277-0.
- Gokhale, Y.; Mehta, R.; Karnik, N.; Kulkarni, U.; Gokhale, S. Tocilizumab improves survival in patients with persistent hypoxia in severe COVID-19 pneumonia. *EclinicalMedicine* **2020**, *24*, 100467, doi:10.1016/j.eclinm.2020.100467.
- Guaraldi, G.; Meschiari, M.; Cozzi-Lepri, A.; Milic, J.; Tonelli, R.; Menozzi, M.; Franceschini, E.; Cuomo, G.; Orlando, G.; Borghi, V.; et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. *Lancet Rheumatol.* **2020**, *2*, e474–e484, doi:10.1016/s2665-9913(20)30173-9.
- Mady, A., et al., Tocilizumab in the treatment of rapidly evolving COVID-19 pneumonia and multifaceted critical illness: A retrospective case series. *Ann Med Surg (Lond)*, 2020. 60: p. 417–424.
- Moreno-García, E., et al., Tocilizumab is associated with reduced risk of ICU admission and mortality in patients with SARS-CoV-2 infection. *medRxiv*, 2020: p. 2020.06.05.20113738.
- Colaneri, M.; Bogliolo, L.; Valsecchi, P.; Sacchi, P.; Zuccaro, V.; Brandolino, F.; Montecucco, C.; Mojoli, F.; Giusti, E.M.; Bruno, R.; et al. Tocilizumab for Treatment of Severe COVID-19 Patients: Preliminary Results from SMAtteo COvid19 REgistry (SMACORE). *Microorg.* **2020**, *8*, 695, doi:10.3390/microorganisms8050695.
- Klopfenstein, T.; Zayet, S.; Lohse, A.; Balblanc, J.-C.; Badie, J.; Royer, P.-Y.; Toko, L.; Mezher, C.; Kadiane-Oussou, N.; Bossert, M.; et al. Tocilizumab therapy reduced intensive care unit admissions and/or mortality in COVID-19 patients. *Médecine et Maladies Infectieuses* **2020**, *50*, 397–400, doi:10.1016/j.medmal.2020.05.001.
- Gordon, A.C., et al., Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. *N Engl J Med*, 2021. 384(16): p. 1491–1502.
- RosasI.O.; BräuN.; WatersM.; GoR.C.; HunterB.D.; BhaganiS.; SkiestD.; AzizM.S.; CooperN.; DouglasI.S.; et al. Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia. *New Engl. J. Med.* **2021**, *384*, 1503–1516, doi:10.1056/nejmoa2028700.
- SalamaC.; HanJ.; YauL.; ReissW.G.; KramerB.; NeidhartJ.D.; CrinerG.J.; Kaplan-LewisE.; BadenR.; PanditL.; et al. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. *New Engl. J. Med.* **2021**, *384*, 20–30, doi:10.1056/nejmoa2030340.
- EimerJ.; VesterbackaJ.; SvenssonA.; StojanovicB.; WagrellC.; SönnernborgA.; NowakP. Tocilizumab shortens time on mechanical ventilation and length of hospital stay in patients with severe COVID-19: a retrospective cohort study. *J. Intern. Med.* **2021**, *289*, 434–436, doi:10.1111/joim.13162.
- KhamisF.; MemishZ.; Al BahraniM.; Al NummaniH.; Al RaisiD.; Al DowaiqiS.; ChhetriS.; Al FahdiF.; Al YahyaiM.; PandakN.; et al. The Role of Convalescent Plasma and Tocilizumab in the Management of COVID-19 Infection: A Cohort of 110 Patients from a Tertiary Care Hospital in Oman. *J. Epidemiology Glob. Heal.* **2021**, *11*, 216–223, doi:10.2991/jegh.k.201222.001.

- 
25. Hermine, O., et al., Effect of Tocilizumab vs Usual Care in Adults Hospitalized With COVID-19 and Moderate or Severe Pneumonia: A Randomized Clinical Trial. *JAMA Intern Med*, 2021. 181(1): p. 32–40.
  26. (CDC), C.f.D.C.a.p. Defining Adult Overweight & Obesity. 2021 June 7, 2021 [cited 2021 October 11]; Available from: <https://www.cdc.gov/obesity/adult/defining.html>.