

Supplementary Table 3: Studies Reporting Secondary Infections in COVID-19 Patients Treated with Tocilizumab

Author/ Year	Study Design/ Population	Intervention	Secondary Infections	Follow-up Duration	Secondary Infection Definition	Comments
Alattar et al. 2020 ⁶⁹	Retrospective case series 25 ICU patients	TCZ IV Dose: Median 5.7mg/kg (IQR 4.8-9.5) Duration: Median 1 dose (IQR 1-3)	4/25 (16%) developed bacterial PNA	14 days	Not reported	Short follow-up duration
Campochiaro et al 2020 ⁷⁰	Retrospective case-control study 65 hospitalized patients 32 (49%) received TCZ	TCZ IV Dose: 400mg/dose Duration: 1 or 2 doses	4/32 (12.5%) developed BSI 1 patient developed candidemia and invasive pulmonary aspergillosis	28 days	No reported	BSI developed anywhere from 8-13 days after treatment
Vu et al 2020 ⁷¹	Retrospective case series 60 hospitalized patients, 75% admitted to ICU	TCZ IV Dose: 400mg (n=47), 600mg (n=13) Duration: 1 dose (n=57), 2 doses (n=3)	16/60 (26.7%) developed secondary infections 48.3% BSI 48.3% PNA	30 days	Not reported	10/16 (62.5%) received concomitant corticosteroids Median time to infection was 10.5 days (range 2-28 days)
Guaraldi et al 2020 ⁷²	Retrospective cohort study 544 hospitalized patients 179 (32.9%) received TCZ	TCZ IV or SQ vs. SOC Dose: 8mg/kg IV (max 800mg/dose), 324mg SQ Duration: 2 doses IV, 1 dose SQ	New infection: 13% vs. 4% (p<0.0001)	Not reported	Not reported	Infections included BSI, PNA, HBV and HSV-1 reactivation
Toniati et al 2020 ⁷⁴	Single-center, prospective case series 100 hospitalized patients, 43% admitted to ICU	TCZ IV Dose: 8mg/kg (max 800mg/dose) Duration: 2 doses, optional 3 rd dose	2 cases of septic shock resulting in mortality	10 days	Not reported	Non-severe secondary infections not reported Short follow-up duration
Biran et al. 2020 ⁷³	Multi-center retrospective cohort study 764 ICU patients 210 (27%) received TCZ	TCZ IV vs. SOC Dose: 400mg/dose Duration: 1 dose, optional 2 nd dose	17% vs. 13% BSI: 9% vs. 8% PNA: 12% vs. 7%	Median of 22 days	Positive blood or sputum cultures	Overall rate of infection was low for critically ill cohort
Rossotti et al 2020 ⁸⁷	Single-center, retrospective cohort study 222 hospitalized patients 74 (33%) received TCZ	TCZ IV vs. SOC Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	32.4% developed infection 78% of infections occurred in critically ill patients	Not reported	Not reported	No statistical comparison to standard of care group for infection

Somers et al 2020 ⁷⁶	Retrospective, single-center cohort study 154 mechanically ventilated patients 78 (51%) received TCZ	TCZ IV vs. SOC Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	54% vs. 26%; p<0.001 VAP: 45% vs. 20%; p<0.001 BSI: 14% vs. 9%; p=0.34	Median of 47 days	Positive respiratory and blood culture >48h after hospitalization assessed by infectious disease physician	Overall, only 25% of patients received corticosteroids <i>Staph aureus</i> was most common cause of VAP
Giacobbe et al 2020 ⁴¹	Retrospective, single-center cohort study 78 ICU patients 18 (23%) received TCZ	TCZ IV Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	40% developed BSI TCZ alone: HR 1.07 (0.38-3.04) TCZ + steroids: HR 10.7 (2.71-42.17)	Discharge or death	BSI defined as at least one positive blood culture >48h after ICU admission Coagulase-negative staphylococci required two consecutive blood cultures with same organism	Methylprednisolone was administered at 1mg/kg Follow-up past 12 days available for <33% of patients
Lewis et al 2020 ⁷⁷	Multi-center, retrospective, cohort study 3580 hospitalized patients 497 (13.9%) received TCZ	TCZ IV vs. SOC Dose: 400mg Duration: 1 dose	34.4% vs. 10.7%, OR 4.18 (2.72-6.52) BSI: 13.9% vs. 3.6%; OR 3.85 (2.08-7.46) PNA: 25.9% vs. 5.8%; OR 5.96 (3.47-10.66)	Not reported	Not reported	Median time to infection was 10 days in TCZ group
Hermine et al 2020 ⁷⁸	Multi-center, open-label, randomized trial CORIMUNO-19 131 non-intubated patients 64 (49%) received TCZ	TCZ IV vs. SOC Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	3.1% vs. 19.4%	28 days	Not reported	Bacterial sepsis and fungal sepsis were only reported
Salvarani et al 2020 ⁷⁹	Multi-center, open-label, randomized trial RCT-TCZ-COVID-19 126 non-intubated patients 60 (48%) received TCZ	TCZ IV vs. SOC Dose: 8mg/kg (max 800mg/dose) Duration: 2 doses	1.7% vs. 6.3%	14 days	Not reported	Short follow-up duration
Stone et al 2020 ⁶⁰	Multi-center, randomized, double-blind, placebo-controlled trial BACC Bay 243 non-intubated patients 161 (66%) received TCZ	TCZ IV vs. placebo Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose	8.1% vs. 17.1%; p=0.03	28 days	Not reported	Non-severe secondary infections not reported 13.7% vs. 1.2% developed severe neutropenia
Gordon et al 2021 ⁸⁰	Multi-center, randomized, double-blind, placebo-controlled trial REMAP-CAP 755 ICU patients	TCZ IV vs. placebo Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	1 serious secondary bacterial infection in TCZ group	21 days	Not reported	Non-severe secondary infections not reported

	353 (47%) received TCZ					
Salama et al 2021 ⁶¹ EMPACTA	Multi-center, randomized, double-blind, placebo- controlled trial 377 non-intubated patients 249 (66%) received TCZ	TCZ IV vs. placebo Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	12.6% vs. 10%	60 days	Not reported	Types of infections were not classified
Rosas et al 2021 ³	Multi-center, randomized, double-blind, placebo- controlled trial 438 hospitalized patients 294 (67.1%) received TCZ	TCZ IV vs. placebo Dose: 8mg/kg (max 800mg/dose) Duration: 1 dose, optional 2 nd dose	21% vs. 25.6% PNA: 2.4% vs. 2.8% BSI: 0.7% vs. 2.1%	28 days	Not reported	

TCZ=tocilizumab, SOC=standard of care, BSI=bloodstream infection, PNA=pneumonia, VAP=ventilator-associated pneumonia, HBV=hepatitis B virus,
HSV=herpes simplex virus