Secondary Infection due to Tocilizumab and Baricitinib in Hospitalized COVID-19 Patients

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BACKGROUND

- Tocilizumab and baricitinib were investigated early in the pandemic as potential agents to supplement standard of care (SOC) for select patients.
- The REMAP-CAP study showed that tocilizumab does not result in a higher incidence of serious adverse events (1 patient had a serious secondary bacterial infection).
- COV-Barrier (baricitinib) study showed 15% patients (110/750) experienced a serious adverse event with serious infections being 9% (64/750).

OBJECTIVE

- To assess secondary infection development due to tocilizumab and baricitinib administration in hospitalized COVID-19 pneumonia patients at two hospitals within the Barnes-Jewish Christian (BJC) healthcare system, Memorial Hospital Belleville & Shiloh

METHODS

Study Design

- Retrospective study that used EPIC database to gather patient information at Memorial Hospital Belleville & Shiloh

Inclusion Criteria

- Adults aged 18 years and older
- Hospitalized due to COVID-19 between May 1st, 2021, and November 30th, 2021
- Received either tocilizumab 8 mg/kg (max 800 mg) for 1 dose or baricitinib 4 mg daily (renally dosed) for 14 days or up to discharge from hospital

Study Measures

- Primary Outcome: If a patient developed a secondary infection within 14 days from tocilizumab or baricitinib administration for the diagnosis of COVID-19 pneumonia
- Secondary Outcomes: Number of patients that met BJC criteria for use, in-hospital mortality, and average duration of steroid use in both groups

Study Measures: Dependent Variables

- Study medications (dose & regimen), steroid regimens, pre-existing comorbidities present at admission, immunosuppressive medications prior to admission, severity of disease state, length of stay (LOS), antimicrobials received

Study Measures: Independent Variables

- Age, gender, race, ethnicity, vaccination & smoking status, location of treatment, BJC's criteria for use

Data Collection & Analysis Method

- Demographics, medication administration histories, culture data, past medical history (PMH), labs, vitals, home medication lists, and other pertinent information from physician notes from EPIC were collected, noted, and evaluated.

METHODS

Data Collection & Analysis Method (Cont'd)

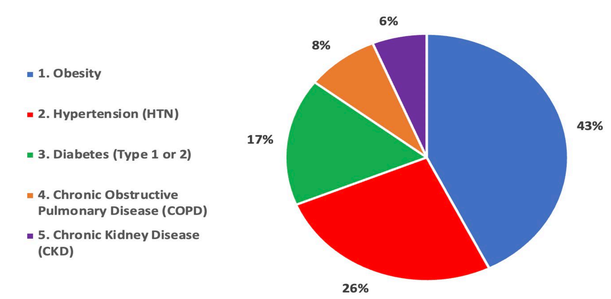
- For each patient: Vaccinated? → Medication? → Meet Criteria? → Dose and duration → culture data → antimicrobials started, reasoning, and duration → steroid regimen → PTA immunosuppressants? → PMH → Secondary infection? → Deceased?
- The data was primarily achieved via summation and percentages. Relative risk (RR) was calculated, and a fisher's exact test was conducted to assess significance.
- 22 tocilizumab patients and 28 baricitinib patients (Total = 50)

RESULTS

Table 1: Baseline Characteristics

Characteristic	Sub-Category	Tocilizumab (n = 22)	Baricitinib (n = 28)	Total (n = 50)
Gender	Male - no. (%)	10 (45.5)	10 (35.7)	20 (40)
	Female - no. (%)	12 (54.5)	18 (64.3)	30 (60)
Age	31 to 50 - no. (%)	2 (9.1)	7 (25)	9 (18)
	51 to 70 - no. (%)	10 (45.5)	12 (42.9)	22 (44)
	71 to 87 - no. (%)	10 (45.5)	9 (32.1)	19 (38)
Race	White - no. (%)	11 (50)	22 (78.6)	33 (66)
	Black - no. (%)	11 (50)	5 (17.9)	16 (32)
	Other - no. (%)	0 (0)	1 (3.6)	1 (2)
Ethnicity	Non-Hispanic - no. (%)	21 (95.5)	26 (92.9)	47 (94)
	Hispanic - no. (%)	0 (0)	1 (3.6)	1 (2)
	Unknown - no. (%)	0 (0)	2 (7.1)	2 (4)
Location	MHB - no. (%)	15 (68.2)	18 (64.3)	33 (66)
	MHE - no. (%)	7 (31.8)	10 (35.7)	17 (34)
Vaccination Status	Vaccinated - no. (%)	5 (22.7)	6 (21.4)	11 (22)
	Unvaccinated - no. (%)	17 (77.3)	20 (71.4)	37 (74)
	Unknown - no. (%)	0 (0)	2 (7.1)	2 (4)
Smoking Status	Current/Former - no. (%)	7 (31.8)	11 (39.3)	18 (36)
	Never Smoked - no. (%)	15 (68.2)	17 (60.7)	32 (64)
Pre-existing Comorbidities of Interest	Obesity - no. (%)	19 (86.4)	22 (78.6)	41 (82)
	Hypertension (HTN) - no. (%)	13 (59.1)	12 (42.9)	25 (50)
	Diabetes (1 or 2) - no. (%)	8 (36.4)	8 (28.6)	16 (32)
	Chronic Obstructive Pulmonary Disease (COPD) - no. (%)	4 (18.2)	4 (14.3)	8 (16)
	Chronic Kidney Disease (CKD) - no. (%)	4 (18.2)	2 (7.1)	6 (12)
	Asthma – no. (%)	2 (9.1)	3 (10.7)	5 (10)
	Coronary Artery Disease (CAD) – no. (%)	2 (9.1)	3 (10.7)	5 (10)
	Stroke/CVD – no. (%)	3 (13.6)	1 (3.6)	4 (8)

Figure 1: Top 5 Pre-Existing Comorbidities



RESULTS

Figure 2: Primary Outcome Results

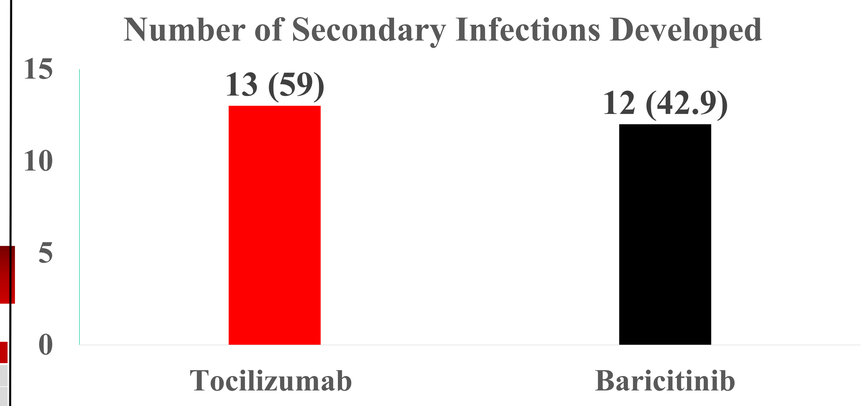


Figure 3: Secondary Outcome Results

Secondary Outcome	Tocilizumab	Baricitinib
Patients Meeting BJC Criteria for Use – n. (%)	22 (100)	28 (100)
In-Hospital Mortality – n. (%)	12 (54.5)	12 (42.9)
Avg. Duration of Steroid Use (Days)	18	15

CONCLUSION

- Secondary infection development is a serious potential adverse event with tocilizumab and baricitinib administration (boxed warning).
- RR = 1.27 (27% higher chance of developing a secondary infection with tocilizumab compared to baricitinib); p = 0.567
- Poor outcomes are common in severe and critical cases of COVID-19 pneumonia.
- Memorial Hospital Belleville and Shiloh expressed 100% compliance with following criteria for use regarding the study medications.
- Based on this study's results, it is difficult to assess the benefit of the study medications in reducing mortality and improving survival.
- More studies with larger sample sizes comparing these two medications are needed to assess which agent is correlated with a higher incidence of secondary infection development.

Limitations

- Sample size
- Definition of secondary infection
- Duration of post-monitoring for baricitinib
- Exclusion criteria – imminent death or likely terminal not excluded