Title: Secondary infection due to tocilizumab and baricitinib in hospitalized COVID-19 patients

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Purpose: Tocilizumab and baricitinib carry a Blackbox Warning for the potential risk of secondary infection development due to their ability to suppress the immune system. However, usage of these therapies has increased immensely as they have been options for hospitalized patients with COVID-19 pneumonia in addition to standard of care. The purpose of this study was to determine the incidence of secondary infection development due to the administration of tocilizumab and baricitinib in hospitalized patients with COVID-19 pneumonia at Memorial Hospital Belleville and Shiloh, Illinois.

Methods: The Belleville Institutional Review Board approved this retrospective chart review study. Patients aged 18 and older who were administered either tocilizumab or baricitinib for COVID-19 pneumonia at either Memorial Hospital Belleville or Memorial Hospital Shiloh were included in this study. The patients evaluated were hospitalized and subsequently administered these therapies between May 1st, 2021 – November 30th, 2022. This study did not identify specific exclusion criteria unless inclusion criteria was not met. Tocilizumab was the first medication of the two to be utilized at Memorial Hospital Belleville and Shiloh, but a shortage occurred resulting in a transition to the use of baricitinib exclusively. This transition occurred in August 2021, so patients who were administered tocilizumab were assessed from May – August and those who were administered baricitinib were assessed from August – November. 22 patients who were administered tocilizumab and 28 patients who were administered baricitinib were included in this retrospective study (n=50). Data was assessed from each patient, specifically demographics, medication history prior to and during admission, culture data, past medical history, labs and vitals, immunization history, and other miscellaneous information from physician notes. The primary outcome was the number of secondary infections that occurred within 14 days of usage of the study medications. This study's definition of a secondary infection was a positive culture result or any antimicrobial initiated within 14 days of medication administration. Secondary outcomes measured were number of patients that met Barnes-Jewish Christian (BJC) criteria for use, average duration of therapy pertaining to steroid use, and in-hospital mortality. Data was achieved via summation and percentages primarily and a relative risk (RR) was calculated. In addition, a Fisher's Exact test was conducted to assess significance.

Results: 13 of the 22 patients (59%) who were administered tocilizumab and 12 of the 28 patients (42.9%) who were administered baricitinib developed a secondary infection. Two patients in the tocilizumab group experienced a positive culture result due to contaminants and were excluded from the primary outcome result. Another patient in the baricitinib group experienced a perforated bowel within 14 days of administration and was also excluded from the primary outcome result. All 50 patients met BJC criteria for use, and the average duration of steroid use was 18 days for the tocilizumab group and 15 days for the baricitinib group (average of 16 days for both groups). Lastly, 12 patients in each group died during their hospital admission (48% total mortality rate, 54.5% tocilizumab, 42.9% baricitinib). RR was 1.27 ($p = 0.567$) meaning there existed a 27% higher chance of developing a secondary infection if administered tocilizumab compared to baricitinib.

Conclusion: Previous studies namely the REMAP-CAP and the COV-BARRIER established these two medications on the market for use in patients hospitalized with COVID-19 pneumonia. However, in this small sample size retrospective study, it is difficult to assess the benefit of these medications. Half of all patients developed a secondary infection and there was a total in-hospital mortality rate of 48%. Memorial Hospital Belleville and Shiloh followed strict BJC criteria for use as all patients met criteria appropriately. Limitations of the study were its definition of a secondary infection, small sample size, duration of post-monitoring for baricitinib, and the exclusion criteria. More academic studies are required that compare these two medications to evaluate the true incidence of secondary infections in patients being treated for COVID-19 pneumonia in the hospital setting.