Title: The Effect of Shifting Preferred Anti-Pseudomonal Pneumonia Coverage on Clinical Outcomes and Safety

Background: Piperacillin/tazobactam (TZP) and cefepime (FEP) are frequently used to treat community and healthcare-associated infections. The current Infectious Diseases Society of America (IDSA) guidelines suggest the use of TZP or FEP for the treatment of hospital acquired pneumonia (HAP), ventilator associated pneumonia (VAP), and community acquired pneumonia (CAP) in patients with *Pseudomonas aeruginosa* risk factors. Few studies have compared TZP and FEP in treatment of pneumonia. Saint Luke's Health System recently shifted its preferred anti-pseudomonal agent from TZP to FEP. This change was due to similar susceptibilities on our antibiogram, dosing convenience, potential lower risk of AKI in combination with vancomycin, as well as a nearly 60% lower daily administration cost. The objective of this study is to compare the clinical outcomes and incidence of adverse events of TZP and FEP for the treatment of pneumonia.

Methods: This is a retrospective cohort study comparing the safety and efficacy of TZP and FEP for the treatment of patients diagnosed with pneumonia at Saint Luke's Health System (SLHS). This study was approved through Saint Luke's institutional review board. Data were pulled on patients admitted from December 1, 2018 to December 31, 2018 who received TZP and patients admitted December 1, 2019 to December 31, 2019 who received FEP for pneumonia. The inclusion criteria for this study are as follows: at least 18 years old, have had a confirmed or presumed pneumonia diagnosis within SLHS, and received FEP or TZP as an empiric therapy for the treatment of pneumonia. The exclusion criteria for this study are as follows: started treatment at a hospital outside SLHS, treated for less than 24 hours with FEP or TZP, treated with antibiotics for less than 5 days, or deemed palliative or comfort care while on FEP or TZP. The primary endpoint is clinical improvement at 7 days. Secondary endpoints include: time to clinical improvement, in-hospital all-cause mortality, time to death, incidence of AKI per the KDIGO criteria, length of hospital stay, length of ICU stay (if applicable), duration of mechanical ventilation (if applicable), need for escalation of antibiotics 48 hours after initiation, time to escalation of antibiotics, subsequent receipt of invasive or non-invasive mechanical ventilation after 48 hours of antibiotic initiation, readmission due to recurrent pneumonia or infectious complications of pneumonia at 30 days, discontinuation of FEP or PTZ due to adverse drug events, and incidence of *Clostridiodes difficile* infection.

Results: A total of 87 patients were included in the analysis. The median age of patients was 73 (27-96) years and 37 (42.5%) were female. The average baseline Charlson Comorbidity Index was 6.08 (5.58 in TZP group versus 6.62 in FEP group) and a total of 33 (37.9%) patients were admitted to the ICU, 18 in TZP group versus 15 in FEP group. There were 33 (73.3%) patients in the TZP group that met the primary endpoint of clinical improvement at 7 days versus 26 (61.9%) in the FEP group (p=0.254). There were no statistically significant differences between groups in regard to any secondary endpoints.

Conclusions: When comparing TZP to FEP for the empiric treatment of pneumonia, no difference was seen in the primary outcome of clinical improvement at 7 days, but our sample lacked the size necessary to determine non-inferiority.