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P2468 Association with 30-day mortality and MIC in patients treated with piperacillin/tazobactam for *Escherichia coli* and *Klebsiella pneumoniae* bloodstream infections that are non-susceptible to ceftriaxone from patients enrolled in the MERINO trial

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Background: The MERINO trial was an international randomized controlled trial comparing piperacillin/tazobactam (PTZ) and meropenem (MER) for treatment of ceftriaxone non-susceptible *E. coli* and *K. pneumoniae* isolated from bloodstream infections. Non-inferiority in the PTZ arm was not demonstrated in comparison to the MER arm. The aim of this study was to determine the relationship of minimum inhibitory concentration (MIC) performed by broth microdilution (BMD) to 30-day mortality for patients treated with PTZ.

Materials/methods: MIC testing was performed by BMD using custom made Sensititre plates (Thermo Fisher) with a PTZ range between 1 µg/ml and 128 µg/ml. Isolates were assessed as susceptible by EUCAST (v8.0; ≤ 8 µg/mL) and CLSI (M100-ED28:2018; ≤ 16 µg/mL) breakpoint tables. Binary recursive partitioning methodology, classification and regression tree (CART) modelling was performed to determine susceptibility breakpoints related to 30-day mortality. Logistic regression was performed to assess for association with 30-day mortality for both log2 MIC and the CART predicted susceptible breakpoint in a bivariate and multivariate model.

Results: 321 isolates from individual enrolled patients were tested from 378 patients in the primary population. 18 deaths occurred amongst 157 patients in the PTZ arm compared to 6 amongst 164 patients in the MER arm (11.5% vs 3.7%). 17.8% and 6.4% of isolates were non-susceptible to PTZ by EUCAST and CLSI susceptible breakpoints respectively. CART regression demonstrated a statistically significant difference related to 30-day mortality at a susceptible clinical breakpoint of ≤ 16µg/mL (p = 0.002). Bivariate regression for log2 MIC did not demonstrate a statistically significant association with mortality (OR 1.2, 95% CI 0.9 - 1.6; p = 0.2), however an association was present with a non-susceptible breakpoint of > 16µg/mL (OR 10.3, 95 CI 2.6 – 41.9; p < 0.001). Adjusting for confounders (Charlson Comorbidity index and UTI source), the non-susceptible > 16µg/mL breakpoint remained statistically significant (aOR 2.0, 1.3 – 3.4; p = 0.002).

Conclusions: The microbiologic mITT analysis, performed using broth microdilution method, demonstrated an association with 30-day mortality at a breakpoint of > 16µg/mL for PTZ by both CART and multivariate logistic regression.

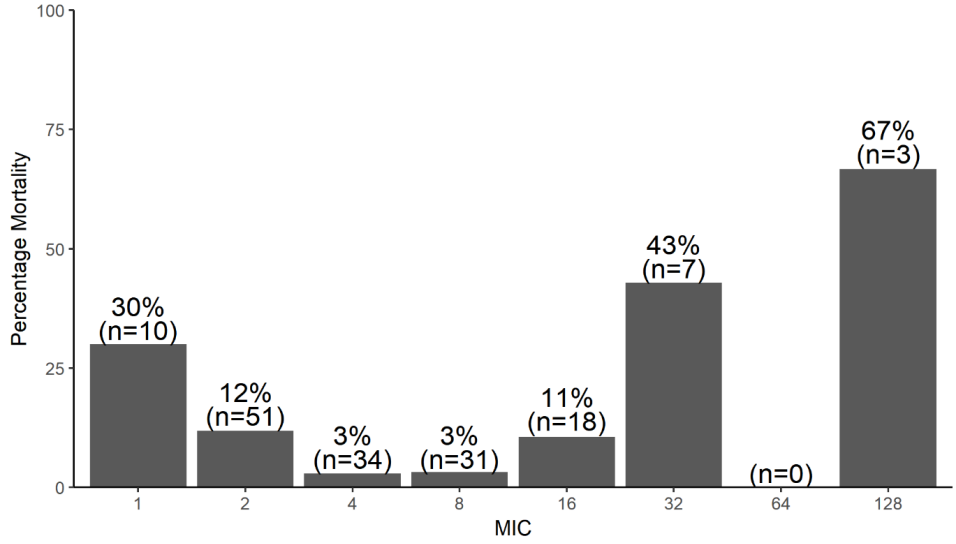

Figure 1. Percentage mortality in piperacillin-tazobactam arm stratified by MIC.