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Ceftazidime-avibactam for the treatment of carbapenemase-producing *Enterobacteriaceae* bacteraemia in oncohaematological patients: calm after the storm

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Background: There are no studies published demonstrating that treatment with ceftazidime-avibactam (CA) for carbapenemase-producing Enterobateriaceae bacteraemia (CPEB) improves survival in patients with hematologic malignancies and neutropenia.

Materials/methods: Prospective observational study performed from May 2014 to August 2019. Adult patients with hematologic malignancies or hematopoietic stem cell transplantation and KPC or OXA48-CPEB were included from 12 centers of Argentina. We compared patients who received definitive treatment with CA with patients treated with other antibiotics (OA). The 30-day mortality was examined by the Kaplan-Meier method with the log-rank test, and the Cox regression model was used to test statistical significance.

Results: 110 patients were included (CA: 22 and OA: 88). No differences were observed in baseline characteristics between CA and OA respectively: age 47 years (37-60) vs 50 years (39-64) (p=0.53); acute leukemia 68.2% vs. 59.1% (p=0.43); neutropenia 81.8% vs 84.1% (p=0.79); high risk by MASCC score: 100% vs 94.6% (p=0.31); neutropenia duration > 10 days: 81.8% vs 84.1% (p=0.79); Charlson score 2 (2-2) vs 2 (2-3) (p=0.27); Pitt score 0 (0-1) vs 1 (0-2) (p=0.11); APACHE II score: 13 (11-20) vs 12 (8-17) (p=0.092). There were no differences in clinical presentation and microbiological characteristics between CA and OA respectively: bacteremia with a clinical source: 68.2% vs. 62.5% (p=0.62); hypotension: 22.7% vs. 36.4% (p=0.31); KPC-CPEB: 95.5% vs 92% (p= 0.58); *Klebsiella* spp.: 90.9% vs. 90.9% (p=1); colistin-resistance: 27.3% vs. 31.8% (p=0.68); Meropenem MIC ≥ 16: 68.2% vs 69.9% (p=0.88). Treatment and outcome between CA and OA were respectively: appropriate empirical treatment: 81.8% (64% received CA) vs 52.3% (p=0.015); combined definitive treatment: 63.6% vs 92% (p=0.001); 7-day clinical response: 86.4% vs 52.3% (p=0.004); ICU admission: 18.2% vs 43.3% (p=0.048); 30-day mortality 18.2% vs. 50% (p=0.008). In the multivariate analysis the factors significantly associated with mortality were: Pitt score: OR 1.3, 95% CI, 1.1-1.45 (p=0.0001) and breakthrough CPEB: OR 2.1, 95% CI, 1.2-3.8 (p=0.011), while definitive treatment with CA was a protector factor for survival: OR 0.34, 95% CI, 0.12-0.9 (p=0.049).

Conclusions: Oncohematological patients with CPEB receiving definitive treatment with CA had clinical and survival benefit over OA treatments.

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