Characterization of β-Lactam Resistance Mechanisms among Baseline Pseudomonas aeruginosa from 5 Ceftazidime-Avibactam Phase 3 Clinical Trials

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Introduction

- Ceftazidime-avibactam, a novel β-lactam/β-lactamase inhibitor, was evaluated in Phase 3 trials for the treatment of complicated urinary tract infection (cUTI), complicated intra-abdominal infection (cIAI), and hospital-acquired pneumonia (HAP). Evaluating ventilator-associated pneumonia (VAP) was considered outside of the scope of the development program, including in the US; however, the European Medicines Agency (EMA) for treating VAP

- The study presented here was carried out to characterize the β-lactam resistance mechanisms in Pseudomonas aeruginosa from patients enrolled in 5 Phase 3 trials of ceftazidime-avibactam.

Materials and Methods

Patients and clinical isolates

- A total of 501 baseline β-lactam-resistant isolates (1 per patient) were screened for susceptibility against comparator agents were interpreted using CLSI breakpoints.

- The transcription levels of the chromosomal β-lactamase were measured by transcriptome analysis. TheompD expression was not altered in the presence of β-lactamase inhibitors, but increased in the presence of β-lactamase inhibitors.

- All amplicons generated were sequenced on both strands (Sanger method); and MIC values were determined. Conclusions

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