

7th Annual Summit on

MICROBIOLOGY: EDUCATION, R&D AND MARKET

September 28-29, 2018 | San Antonio, USA

***In vitro* induction of bacterial resistance to Ceftazidime-avibactam and investigation of the resistance mechanisms**

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Ceftazidime-avibactam antibiotic agent is a compound of third-generation cephalosporin ceftazidime and a novel non- β -lactam β -lactamase inhibitor avibactam. Avibactam was approved for use in the United States in 2015. It is an active inhibitor of class A, class C, and some class D enzymes. A few clinical studies have been conducted to study the overall effect of avibactam against carbapenem-resistant Enterobacteriaceae (CRE) that produce *Klebsiella pneumoniae* carbapenemase (KPC). To date, no studies on the antimicrobial activity of the combination against *Salmonella* species have been published. In this study, we looked at the impact of adding avibactam to ceftazidime to treat ceftazidime-resistance *Salmonella. Senftenberg* (that produce TEM and or OXA). The primary goal of this examination was to determine if ceftazidime-avibactam can induce resistance in bacteria after long-term exposure to the combination. We employed a selection method of the combination and avibactam alone for *S. Senftenberg*. We monitored bacterial resistance, characterized the stability and cross-resistance. The combination was very effective against the *S. Senftenberg*, the addition of avibactam resulted in a significant increase in ceftazidime activity, with MICs generally reduced from 512 to 4 μ g/ml. *S. Senftenberg* evolved resistance to the combination and to avibactam alone under long-term selection pressure with continuously increasing concentrations of drugs. Cross-resistance of the induced strains to other antimicrobial agents (ampicillin and ciprofloxacin) was observed. Our results indicated that resistance to the combination could be formed at 5-fold (higher than 1/2 the MIC). Highly resistant bacteria at 10-fold was isolated for further analysis. Our undergoing aim is to investigate the potential role of beta-lactamase and other enzymes in resistance mechanism using RNA sequencing. Most importantly, our preliminary results raise serious attention concerning the long-term risks correlated with the development and clinical use of ceftazidime-avibactam.

Biography

Yosra Modafer is a PhD student at Tennessee State University. She has her expertise in studying resistance mechanisms to the antibiotic. She also has her master research in investigating the effect of Miswak (which is a natural wood stick has been used many years ago in Asia and Africa to clean oral teeth and believed to have antimicrobial activity) on the oral microbes using saliva samples from 18 volunteers (in 2015).

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