Evaluation of Avibactam Combined With β-Lactams Against Non-tuberculous Mycobacteria

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Background. Nontuberculous mycobacteria (NTM), defined as any mycobacterial pathogen other than Mycobacterium tuberculosis, are a diverse group of pathogens that collectively cause substantial but often unappreciated illness worldwide. As a result of their intrinsic resistance to M. tuberculosis drugs and general antibiotics, there are limited treatment options against NTM infections. β-lactams have not been routinely used against NTMs due to intrinsic resistance, caused in some by chromosomally-encoded β-lactamases. The recent approval of avibactam (AVI), a non-β-lactam, β-lactamase inhibitor raises the possibility that its use in combination with a β-lactam might have activity against NTMs.

Methods. In the current study, we tested the in vitro activity of ceftaroline (CPT, a broad-spectrum cephalosporin), ceftazidime (CAZ, a third-generation cephalosporin), and aztreonam (ATM, a monobactam) with and without AVI, against 12 recent clinical isolates including Mycobacterium abscessus (4), Mycobacterium fortuitum (4), Mycobacterium marinum (2), Mycobacterium avium (1) and Mycobacterium smegmatis (1). Using a micro-dilution assay with 7H10 media, a range of drug concentrations from 2 to 512 µg/mL, was evaluated with and without AVI at a constant concentration of 4 µg/mL.

Results. ATM and CAZ, alone or in combination with AVI were ineffective against the different NTM species with most MICs >32 µg/mL. In contrast, CPT activity ranged from 8–16 µg/mL for most of the isolates and in combination with AVI, the MIC was generally lowered, including to MICs <4 µg/mL against 5 isolates.

Conclusion. These findings provide evidence that with a suitable β-lactam, AVI can reduce MICs against the majority of the NTM species and they justify the inclusion of these emerging pathogens in screens that assess novel β-lactamase inhibitors.

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