Activity of Aztreonam Combined with the Beta-lactamase Inhibitor Avibactam Tested against Metallo-β-lactamase-producing Organisms

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Abstract

Objective: To evaluate in the vitro activity of aztreonam (ATM) against a collection of metallo-β-lactamase (MBL)-producing Enterobacteriaceae spp. The emergence of MBL-producing Enterobacteriaceae spp. and the development of resistance to multiple antimicrobial agents has led to the search for alternative treatment options for infections caused by MBL-producing organisms.

Methods: A total of 133 MBL-producing Enterobacteriaceae spp. isolates were collected from Europe and North America. All the isolates were tested for MBL production using the phenotypic assay CLSI for MBL. ATM was tested against each MBL-producing isolate using CLSI broth microdilution and was compared to ATM with Avibactam (ATM-AVI) combination. All other compounds exhibited very limited activity compared to ATM-AVI. The activities of ATM-AVI against metallo-β-lactamase producing organisms (ATM-MBL) and Metallo-β-lactamase-producing Gram-negative bacteria were compared to ATM-AVI by determining the minimum inhibitory concentration (MIC) values. The results were compared to the CLSI breakpoints for ATM.

Materials and Methods

Antimicrobial agent MIC50 MIC90 Range
Aztreonam - - - - - - - - - - - -
Aztreonam-avibactam - - - - - - - - - - - -
Aztreonam - - - - - - 1(2.1) 5(12.8) 4(21.3) 15(53.2) 7(68.1) 7(83.0) 8(100.0)
Aztreonam - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Aztreonam-avibactam 3(11.5) 7(38.5) 5(57.7) 4(73.1) 4(88.5) 1(92.3) 2(100.0) - - - - - -
Ceftazidime - - - - - - - - - - - -
Ceftazidime-avibactam - - - - - - - - - - - -
Ceftazidime - - - - - - 1(2.3) 5(13.6) 4(22.7) 15(56.8) 4(65.9) 7(81.8) 8(100.0)
Ceftazidime - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Ceftazidime-avibactam - - - - - - 1(4.3) 2(13.0) 4(30.4) 10(73.9) 4(91.5) 0(91.5) 2(100.0)
Ciprofloxacin - - - - - - - - - - - -
Ciprofloxacin-avibactam - - - - - - - - - - - -
Ciprofloxacin - - - - - - 1(2.5) 5(14.3) 4(22.7) 15(56.8) 4(65.9) 7(81.8) 8(100.0)
Ciprofloxacin - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Ciprofloxacin-avibactam - - - - - - 1(1.8) 2(11.1) 4(28.6) 10(73.9) 4(91.5) 0(91.5) 2(100.0)
Imipenem - - - - - - - - - - - -
Imipenem-avibactam - - - - - - - - - - - -
Imipenem - - - - - - 1(2.4) 5(14.3) 4(22.7) 15(56.8) 4(65.9) 7(81.8) 8(100.0)
Imipenem - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Imipenem-avibactam - - - - - - 1(1.8) 2(11.1) 4(28.6) 10(73.9) 4(91.5) 0(91.5) 2(100.0)
Meropenem - - - - - - - - - - - -
Meropenem-avibactam - - - - - - - - - - - -
Meropenem - - - - - - 1(2.4) 5(14.3) 4(22.7) 15(56.8) 4(65.9) 7(81.8) 8(100.0)
Meropenem - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Meropenem-avibactam - - - - - - 1(1.8) 2(11.1) 4(28.6) 10(73.9) 4(91.5) 0(91.5) 2(100.0)
Tigecycline - - - - - - - - - - - -
Tigecycline-avibactam - - - - - - - - - - - -
Tigecycline - - - - - - 1(2.5) 5(14.3) 4(22.7) 15(56.8) 4(65.9) 7(81.8) 8(100.0)
Tigecycline - - 3(12.0) 1(16.0) 2(24.0) 1(28.0) 2(36.0) 0(36.0) 0(36.0) 2(44.0) 3(56.0) 5(76.0) 6(100.0)
Tigecycline-avibactam - - - - - - 1(1.8) 2(11.1) 4(28.6) 10(73.9) 4(91.5) 0(91.5) 2(100.0)

Introduction

The emergence of acquired metallo-β-lactamases (MBLs) among important pathogens, including nosocomial pathogens such as Enterobacteriaceae spp., Pseudomonas aeruginosa, and Acinetobacter spp., has highlighted a significant clinical problem that is currently being aggravated by the widespread dissemination of MBL-producing strains, which are often resistant to β-lactam agents. Non-β-lactamase enzymes such as β-lactamases, which are enzymes that are resistant to β- lactams, have emerged as major contributors to the development of resistance to β-lactams. The phenomenon of MBL production is a major concern for public health due to the development of resistance to β-lactams and the lack of alternative treatment options.

Results

The emergence of acquired metallo-β-lactamases (MBLs) among important pathogens, including nosocomial pathogens such as Enterobacteriaceae spp., Pseudomonas aeruginosa, and Acinetobacter spp., has highlighted a significant clinical problem that is currently being aggravated by the widespread dissemination of MBL-producing strains, which are often resistant to β-lactam agents. Non-β-lactamase enzymes such as β-lactamases, which are enzymes that are resistant to β- lactams, have emerged as major contributors to the development of resistance to β-lactams. The phenomenon of MBL production is a major concern for public health due to the development of resistance to β-lactams and the lack of alternative treatment options.

Conclusions

- Aztreonam-avibactam was very active against this large collection of metallo-β-lactamase-producing Enterobacteriaceae spp., regardless of the bacterial species or type of metallo-β-lactamase.
- Aztreonam-avibactam activity against metallo-β-lactamase-producing Pseudomonas aeruginosa and Acinetobacter spp. was more similar to that of ATM when tested alone.
- Aztreonam-avibactam was better able to restore aztreonam activity against the vast majority of MBL-producing Enterobacteriaceae spp. in comparison to ATM alone.

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