00615

Activity *in vitro* of new beta-lactam beta-lactamase inhibitor combinations against *Burkholderia cepacia* Complex (Bcc) and *Burkholderia gladioli* (Bgl) isolated from patients with cystic fibrosis

03. Bacterial susceptibility & resistance

3c. Susceptibility testing methods (incl. assay validation, phenotypic assays and comparative studies, excl. TB)

Likely attendance

Onsite

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Background

Bcc and Bgl are opportunistic pathogens that most commonly infect patients with cystic fibrosis (CF) or immunocompromised individuals. This genus is intrinsically multidrug resistant (MDR) rendering treatment of infections due to these species problematic. This study describes *in vitro* activity of imipenem (IMP), imipemem-relebactam (IMR), ceftazidime-avibactam (CAZ-AVI), aztreonam-avibactam (ATM-AVI) and piperacillin-avibactam (PIP-AVI) against Bcc/Bgl clinical isolates recovered from respiratory specimens from individuals with CF.

Methods

From January 2015 through March 2022 a total of 115 Bcc/Bgl clinical isolates were included. Isolates were identified by MALDI-TOF (Vitek® MS). MICs for IMP, IMR, ATM-AVI, CAZ-AVI and PIP-AVI were determined by agar dilution (CLSI method), using fixed concentration of DBOs (4 mg/L). CAZ breakpoints for Bcc and IMP, ATM and PIP breakpoints for *Pseudomonas aeruginosa* were used to assign phenotypes for CAZ-AVI, IMP/IMR, ATM-AVI and PIP-AVI, respectively. *Escherichia coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 700603 and *K. pneumoniae* BAA-1705 were used as QC strains. The Z proportions statistical test was performed.

Results

Species distribution: *B. contaminans* (n=67/115, 58%), B. *cenocepacia* (n=25/115, 22%), *B. gladioli* (n=7/115, 6%), *B. vietnamiensis* (n=6/115, 5%) *B. cepacia* (n=5/115, 4%), *B. multivorans* (n=2/115, 2%), *B. ambifaria* (n=1/115, <1%), *B. stabilis* (n=1/115, <1%), *B. pyrrocina* (n=1/115, <1%). MIC50, MIC90 and MIC ranges for the antimicrobial tested are depicted in Figure 1. IMR and PIP-AVI showed the lower MICs values ($p<0.05$). Isolates were significatively more susceptible to PIP-AVI (98.3%) than comparators ($p<0.05$). IMR resulted superior to CAZ-AVI (susceptible 74.5% vs 62.6%, respectively) ($p<0.05$) (Figure 2). *B. cenocepacia* was less susceptible to IMR than B. contaminans (52% vs 81%, respectively) ($p<0.05$). Two isolates, 1 *B. contaminans* and 1 *B. cenocepacia,* showed cross-resistance to all agents tested.

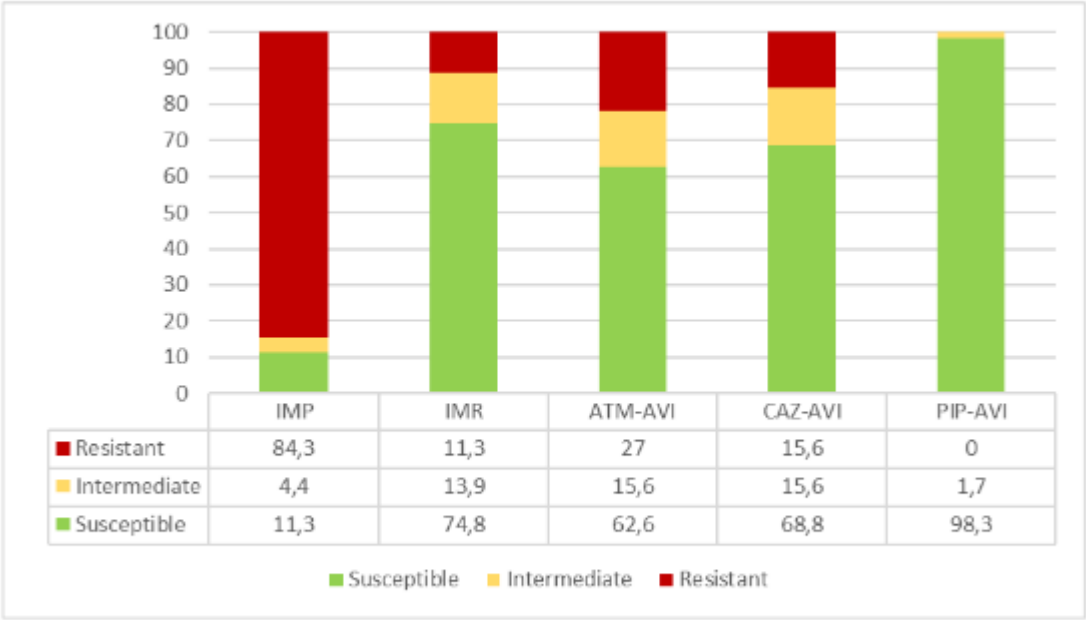
Conclusions

This work described alternative antibiotic combinations to overcome MDR of Bcc/Bgl isolates. Relebactam was highly effective at restoring the susceptibility to imipenem, with only 11.3% of isolates remaining resistant. Among avibactam combinations, PIP-AVI displayed the most potent in vitro activity, followed by CAZ-AVI and finally ATM-AVI. We confirmed that PIP-AVI and IMR could represent alternative antibiotic combinations to overcome MDR typically observed in CF patients.

Figure 1 - MIC_{50}, MIC_{90} and MIC ranges for antimicrobial tested against 115 Bcc/Bgl

MICs in mg/L	IMP	IMR	ATM-AVI	CAZ-AVI	PIP-AVI
MIC_{50}	16	1	8	8	2
MIC_{90}	64	8	32	32	8
MIC ranges	0,5 - 32	0,5 - 8	0,5 - 32	0,5 - 32	0,5 - 32

Figure 2 - *In vitro* activity comparison for antimicrobial tested against 115 Bcc/Bgl



	IMP	IMR	ATM-AVI	CAZ-AVI	PIP-AVI
Resistant	84,3	11,3	27	15,6	0
Intermediate	4,4	13,9	15,6	15,6	1,7
Susceptible	11,3	74,8	62,6	68,8	98,3

Percentage (%) of isolates resistant (red), intermediate (yellow), or susceptible (green) to IMP, IMR, ATM-AVI, CAZ-AVI and PIP-AVI

Keyword 1
New and non-traditional drugs
Keyword 2
Antimicrobial susceptibility testing (AST)
Keyword 3
Cystic Fibrosis

Conflicts of interest

Do you have any conflicts of interest to declare?
No