IDWeek 2022 | Poster #P1686

Antimicrobial Activity of Aztreonam-Avibactam, Ceftazidime-Avibactam, and Comparator Agents against *Pseudomonas aeruginosa* from Cystic Fibrosis Patients

Helio S. Sader, Leonard R. Duncan, Rodrigo E. Mendes, Mariana Castanheira

JMI Laboratories, North Liberty, Iowa, USA

CONCLUSIONS

- ATM-AVI and CAZ-AVI exhibited potent activity against *P. aeruginosa* isolated from CF patients in the US and EU.
- ATM-AVI and CAZ-AVI retained good activity against isolates resistant to other antimicrobials, including MDR and XDR organisms.
- Both ATM-AVI and CAZ-AVI showed greater activity than TOB against *P. aeruginosa* from CF patients.
- ATM-AVI and CAZ-AVI may represent valuable options to treat CF patients with pulmonary exacerbations due to *P. aeruginosa* infection.

Scan QR code or utilize the following link to download an electronic version of this presentation and other AbbVie IDWeek 2022 scientific presentations:

https://abbvie1.outsystemsenterprise.com/GMAEventPublications/Assets.aspx?ConferenceId=440

To submit a medical question, please visit www.abbviemedinfo.com

Contact Information

Helio S. Sader, MD, Ph.D.
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: helio-sader@jmilabs.com

Funding

This study was supported by AbbVie. All authors are employees of JMI Laboratories, which was paid consultant to AbbVie in connection with the development of this poster.

Acknowledgments

The authors thank all participant centers for their work in providing isolates.

References

1. CLSI. 2022. M100Ed32. Performance standards for antimicrobial susceptibility testing; 32nd informational supplement. Clinical and Laboratory Standards Institute, Wayne, PA.
2. Cruil MR, Somayaji R, Ramos KJ *et al.* 2018. Changing rates of chronic *Pseudomonas aeruginosa* infections in cystic fibrosis: A population-based cohort study. Clin Infect Dis 67: 1088-95.
3. Emerson J, Rosenfeld M, McNamara S *et al.* 2002. *Pseudomonas aeruginosa* and other predictors of mortality and morbidity in young children with cystic fibrosis. Pediatr Pulmonol 34: 91-100.
4. Fuhrmeister AS, Jones RN, Sader HS *et al.* 2019. Global Surveillance of antimicrobial resistance: 20 years of experience with the SENTRY Program. Open Forum Infect Dis 6: S1-S102.
5. Magiorakos AP, Srinivasan A, Carey RB, et al, 2012. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 18:268-281.

abbvie

INTRODUCTION

- *Pseudomonas aeruginosa* is the most common cultured respiratory pathogen in individuals with cystic fibrosis (CF) and is associated with a more rapid decline in lung function.
- Aztreonam-avibactam (ATM-AVI) is under clinical development for the treatment of serious infections caused by Gram-negative bacteria, including metallo-β-lactamase (MBL) producers.
- Four other β-lactamase inhibitor combinations (BL/BLI) have been recently approved by the US FDA: ceftazidime-avibactam (CAZ-AVI), ceftolozane-tazobactam (C-T), meropenem-vaborbactam (MEM-VAB), and imipenem-relebactam (IMI-REL).
- We evaluated the *in vitro* activity of these 5 BL/BLIs and comparators against *P. aeruginosa* causing CF pulmonary exacerbation.

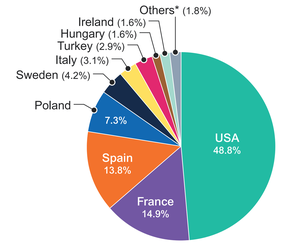
METHODS

- Isolates were collected as part of SENTRY Antimicrobial Surveillance Program.
- Medical centers were asked to collect consecutive bacterial isolates from lower respiratory tract sites of CF patients in 2018–2021.
- Each participant center could contribute up to 40 *P. aeruginosa* isolates.
- Only isolates from invasive sampling, including transtracheal aspiration, bronchoalveolar lavage, protected brush samples, or qualified sputum samples, were accepted.
- The isolate collection included 383 *P. aeruginosa* isolates (1/patient) from 35 medical centers in the US (*n*=187) and 12 centers in Europe (EU; *n*=196; Figure 1).
- Isolates were categorized as multidrug-resistant (MDR) or extensively drug-resistant (XDR) according to criteria defined in 2012 by the joint European and US Centers for Disease Control:
  - MDR: nonsusceptible to ≥1 agent in ≥3 antimicrobial classes.
  - XDR: susceptible to ≤2 classes.
- Isolates were susceptibility tested by the CLSI broth microdilution method (M100; 2022).
- MIC results were interpreted according to CLSI and/or US FDA breakpoints when available.
- A provisional aztreonam-avibactam PK/PD breakpoint of ≤8 mg/L was applied for comparison.
- MEM-VAB is not approved for *P. aeruginosa* treatment in the US; thus, MEM-VAB breakpoints published for Enterobacterales (≤4/8/≥16 mg/L for S/I/R) by CLSI were applied for comparison.

RESULTS

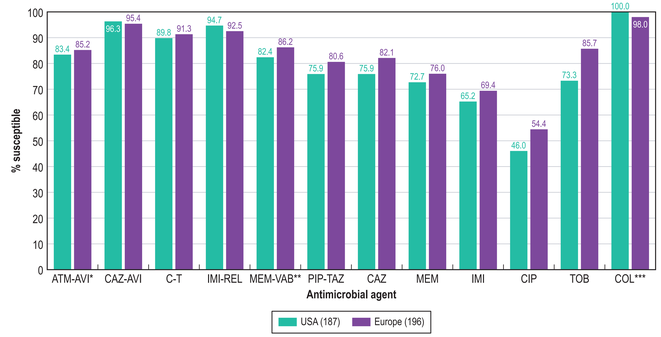
- ATM-AVI ($MIC_{50/90}$, 4/>16 mg/L) inhibited 83.4% and 85.2% of isolates from the US and EU at ≤8 mg/L, respectively (Figure 2).
- CAZ-AVI ($MIC_{50/90}$, 2/8 mg/L; 96.3%/95.4% susceptible [S] in US/EU) was the most active BL/BLI agent, followed by IMI-REL (94.7%/92.5%S in US/EU) and C-T (89.8%/91.3%S in US/EU; Figure 2).
- MEM-VAB ($MIC_{50/90}$, 0.5/8 mg/L; not approved for *P. aeruginosa* in the US) and MEM ($MIC_{50/90}$, 0.5/16 mg/L) showed similar potency (data not shown).
- Tobramycin (TOB)-S rates were 73.3% and 85.7% in US and EU, respectively (Figure 2).
- Among TOB–non-S (NS) isolates, 84.6% were CAZ-AVI–S and 73.1% were inhibited at ATM-AVI MIC of ≤8 mg/L (Figure 3).
- CAZ-AVI retained good activity against C-T–NS (61.1%S), IMI-REL–NS (62.1%S), piperacillin-tazobactam (PIP-TAZ)–NS (86.7%S), meropenem (MEM)–NS (86.6%S), and ciprofloxacin (CIP)–NS (92.1%S) isolates (Figure 3).
- ATM-AVI and TOB showed similar coverage against *P. aeruginosa*–resistant subsets (Figure 3).
- MDR and XDR phenotypes were observed among 40.1%/30.1% and 24.6%/16.8% of isolates from the US and EU, respectively (Figure 4).
- Among MDR isolates, 88.1% were CAZ-AVI–S, 65.7% were inhibited at ≤8 mg/L of ATM-AVI, and 57.5% were TOB-S (Figure 3).
- ATM-AVI and TOB retained activity against 54.4% and 49.4% of XDR isolates, whereas 82.3% of these isolates were CAZ-AVI–S (Figure 3).

Figure 1. Percent distribution of *P. aeruginosa* by country



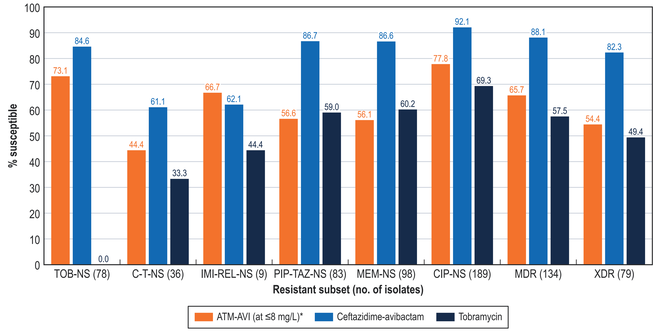
* Include Russia (0.8%), Germany (0.5%), Belgium (0.3%), and Czech Republic (0.3%).

Figure 2. Antimicrobial susceptibility of *P. aeruginosa* isolates from cystic fibrosis patients



* Percentages inhibited at ≤8 mg/L.
** Meropenem-vaborbactam susceptible breakpoint for Enterobacterales (≤4 mg/L) was applied for comparison.
*** Percentage inhibited at ≤2 mg/L (intermediate per CLSI criteria).
Abbreviations: ATM-AVI, aztreonam-avibactam; CAZ-AVI, ceftazidime-avibactam; C-T, ceftolozane-tazobactam; IMI-REL, imipenem-relebactam; MEM-VAB, meropenem-vaborbactam; PIP-TAZ, piperacillin-tazobactam; CAZ, ceftazidime; MEM, meropenem; IMI, imipenem; CIP, ciprofloxacin; TOB, tobramycin; COL, colistin.

Figure 3. Activity of aztreonam-avibactam (ATM-AVI), ceftazidime-avibactam, and tobramycin against resistant subsets of *P. aeruginosa* from cystic fibrosis patients



* Percentages inhibited at ≤8 mg/L.
Abbreviations: TOB, tobramycin; NS, nonsusceptible per CLSI; C-T, ceftolozane-tazobactam; IMI-REL, imipenem-relebactam; PIP-TAZ, piperacillin-tazobactam; MEM, meropenem; CIP, ciprofloxacin; MDR, multidrug-resistant; XDR, extensively drug-resistant; ATM-AVI, aztreonam-avibactam

Figure 4. Frequency of multidrug-resistant (MDR) and extensively drug-resistant (XDR) isolates stratified by geographic region