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Antimicrobial Activity of Aztreonam-Avibactam and Comparator Agents against a Large Collection of *Stenotrophomonas maltophilia* Isolates Collected in United States Medical Centers (2019–2023)

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CONCLUSIONS

Aztreonam-avibactam exhibited potent activity and broad coverage against *S. maltophilia* from US hospitals and its activity was not adversely affected by resistance to other agents.

Our results indicated that aztreonam-avibactam may represent a valuable option to treat *S. maltophilia* infections, addressing a major unmet medical need.

Clinical studies are urgently warranted to evaluate the efficacy of aztreonam-avibactam against infection caused by *S. maltophilia*.

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INTRODUCTION

- Aztreonam-avibactam is under development in the United States (US) to treat infections caused by Gram-negative bacteria, including metallo-β-lactamase (MBL) producers.
- Phase 3 clinical trials REVISIT (NCT03329092) and ASSEMBLE (NCT03580044) evaluated the efficacy, safety, and tolerability of aztreonam-avibactam in treating serious bacterial infections due to Gram-negative bacteria, including MBL-producing multidrug-resistant pathogens for which there are limited or no treatment options.
- Moreover, aztreonam-avibactam has been recently approved by the European Medicine Agency (Emblaveo®) to treat adults who have complicated intra-abdominal infections (IAI), hospital-acquired pneumonia (including ventilator-associated pneumonia), and complicated urinary tract infections (UTI; including pyelonephritis), as well as infections caused by aerobic Gram-negative organisms in patients who have limited treatment options.
- The occurrence of *S. maltophilia* infections has increased continuously in the last few years and there are very limited treatment options for systemic infections caused by this organism.
- We evaluated the *in vitro* activities of aztreonam-avibactam and comparators against a large collection of *S. maltophilia* from US medical centers.

METHODS

- 1,400 clinical isolates were consecutively collected from 62 US medical centers in 2019–2023.
- Infection sites included pneumonia (*n*=1,020; 72.9%), bloodstream infection (*n*=117; 8.4%), skin and skin structure infection (SSSI; *n*=124; 8.9%), and others (*n*=139; 9.9%; Figure 1).
- Only isolates determined to be significant by local criteria as the reported probable cause of infection were included in the study.
- Isolates were susceptibility tested by CLSI M07 broth microdilution methods at a central laboratory.
- Aztreonam-avibactam was tested with avibactam at fixed 4 mg/L and a pharmacodynamic/pharmacokinetic susceptible (S) breakpoint of ≤8 mg/L applied for comparison.

RESULTS

- Aztreonam-avibactam inhibited 99.6% of isolates at ≤8 mg/L ($MIC_{50/90}$, 2/4 mg/L) and demonstrated potent activity against isolates from all infection types (Table 1 and Figure 2).
- Aztreonam-avibactam inhibited 99.7% of isolates from pneumonia, 99.2% of isolates from SSSI, and 100.0% of isolates from BSI and UTI at ≤8 mg/L (Table 1 and Figure 2).
- Aztreonam-avibactam retained potent activity against isolates not susceptible to other agents commonly used to treat *S. maltophilia* infections (Table 2).
- The most active comparator agents were trimethoprim-sulfamethoxazole (TMP-SMX) and minocycline (Table 1 and Figure 3).
- Aztreonam-avibactam was active (MIC ≤8 mg/L) against 100.0% of TMP-SMX-non-susceptible isolates, 99.3% of isolates non-susceptible to minocycline or levofloxacin, and 99.5% of isolates with tigecycline MIC >2 mg/L (Table 2).
- TMP-SMX ($MIC_{50/90}$, ≤0.12/0.5 mg/L) was active against 96.9% of isolates (Table 1 and Figure 3).
- Minocycline ($MIC_{50/90}$, 0.5/2 mg/L) and levofloxacin ($MIC_{50/90}$, 1/8 mg/L) were active against 89.2% and 78.9% of isolates according to the 2024 CLSI breakpoint criteria (Table 1 and Figure 3).

Table 1. Activity of aztreonam-avibactam and comparator agents stratified by infection type

Infection site (no. isolates)	ATM-AVI[a]	% susceptible per 2024 CLSI criteria			Tigecycline[b]
		TMP-SMX	Minocycline	Levofloxacin	
Pneumonia (1,020)	99.7	96.6	89.0	78.6	87.2
SSSI (124)	99.2	97.6	89.4	79.0	89.5
BSI (117)	100.0	99.1	88.8	82.1	85.5
UTI (48)	100.0	100.0	91.9	83.3	89.6
IAI (30)	96.7	93.3	81.5	66.7	66.7
Other infections (61)	100.0	96.7	93.1	80.3	90.2
Total (1,400)	99.6	96.9	89.2	78.9	87.0

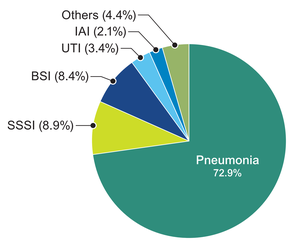
[a] % inhibited at ≤8 mg/L for comparison purpose.
[b] % inhibited at ≤2 mg/L, which is the US FDA susceptible breakpoint for Enterobacterales for comparison.
Abbreviations: ATM-AVI, aztreonam-avibactam; TMP-SMX, trimethoprim-sulfamethoxazole; SSSI, skin and skin structure infection; BSI, bloodstream infection; UTI, urinary tract infection; IAI, intra-abdominal infection.

Table 2. Activity of aztreonam-avibactam against organisms resistant to antimicrobials commonly used to treat *S. maltophilia* infections

Infection / resistant subset (no. isolates)	ATM-AVI[a]	% susceptible per 2024 CLSI criteria			Tigecycline[b]
		TMP-SMX	Minocycline	Levofloxacin	
TMP-SMX-NS (43)[c]	100.0	0.0	51.2	23.3	60.5
Minocycline-NS (141)[c]	99.3	85.8	0.0	15.6	19.9
Levofloxacin-NS (295)[c]	99.3	88.8	55.6	0.0	47.8
Tigecycline MIC >2 mg/L (182)	99.5	90.7	31.1	15.4	0.0

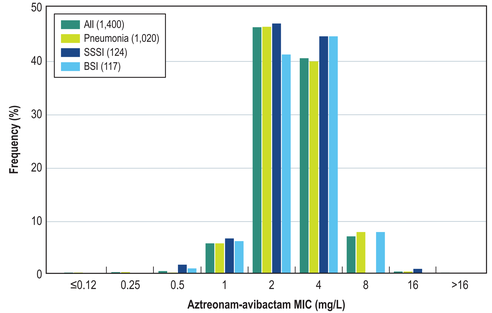
[a] % inhibited at ≤8 mg/L for comparison purpose.
[b] % inhibited at ≤2 mg/L, which is the US FDA susceptible breakpoint for Enterobacterales for comparison.
[c] Isolates not susceptible per CLSI M100 (2024) criteria.
Abbreviations: ATM-AVI, aztreonam-avibactam; TMP-SMX, trimethoprim-sulfamethoxazole; NS, nonsusceptible.

Figure 1. Distribution of *S. maltophilia* isolates by infection sources



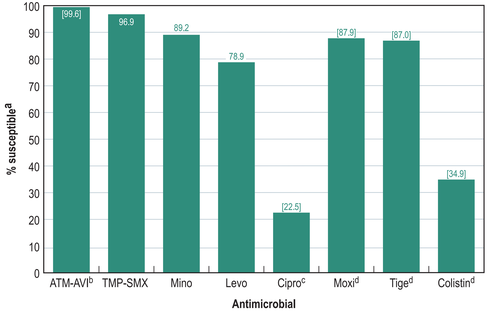
Abbreviations: SSSI, skin and skin structure infection; BSI, bloodstream infection; UTI, urinary tract infection; IAI, intra-abdominal infection.

Figure 2. Aztreonam-avibactam MIC distributions for *S. maltophilia* isolates stratified by selected infection sources



Abbreviations: SSSI, skin and skin structure infection; BSI, bloodstream infection.

Figure 3. Antimicrobial susceptibility of *S. maltophilia* (*n*=1,400) from US medical centers (2019–2023)



[a] Criteria as published by CLSI (2024) and US FDA (2024) unless noted.
[b, c, d] Values in brackets indicate % inhibited at: ≤8 mg/L ([b]), ≤1 mg/L ([c]), and ≤2 mg/L ([d]) for comparison.
Abbreviations: ATM-AVI, aztreonam-avibactam; TMP-SMX, trimethoprim-sulfamethoxazole; Mino, minocycline; Levo, levofloxacin; Cipro, ciprofloxacin; Moxi, moxifloxacin; Tige, tigecycline.