

Evaluation of In Vitro Efficacy of Aztreonam-Nacubactam and Cefepime-Nacubactam Against Clinical Isolates of *Stenotrophomonas maltophilia*

Yoshifumi Uwamino<sup>1</sup>, Wataru Aoki<sup>1</sup>, Hiroaki Kubota<sup>2</sup>, Hiromichi Matsushita<sup>1</sup>  
1. Keio University School of Medicine, Tokyo, Japan 2. Tokyo Metropolitan Institute of Public Health, Tokyo, Japan

Background

- ✓ *Stenotrophomonas maltophilia* harbors L1 metallo-β-lactamase and L2 serine β-lactamase, conferring resistance to most β-lactams.
- ✓ Diazabicyclooctanes (DBOs) such as nacubactam (NAC) have intrinsic antibacterial activity via penicillin-binding protein 2 (PBP2) binding, potentially enhancing β-lactam efficacy even against metallo-β-lactamase (MBL)-producing organisms.
- ✓ The in vitro activity of aztreonam (ATM)-NAC and cefepime (FEP)-NAC against *S. maltophilia* has not been previously evaluated.

Methods

- ✓ We tested 53 blood culture isolates of *S. maltophilia* (2012–2024, Keio University Hospital, Tokyo) by broth microdilution per CLSI M100 (35th ed.).
- ✓ NAC was combined with ATM or FEP at a 1:1 ratio. MIC50/MIC90 values were determined, and differences with/without NAC were analyzed using the Wilcoxon signed-rank test after log transformation.
- ✓ Whole-genome sequencing confirmed sequence types, clonality, and β-lactamase genes.

Results

Isolate number	Sequence type	blaL1	blaL2
S1	Unidentified	✓	✓
S2	28	✓	✓
S3	621	✓	✓
S4	Unidentified		
S5	714	✓	✓
S6	77	✓	✓
S7	Unidentified	✓	✓
S8	77	✓	✓
S9	28	✓	✓
S10	94	✓	✓
S11	94	✓	✓
S12	151	✓	✓
S13	Unidentified	✓	✓
S14	Unidentified	✓	✓
S15	Unidentified	✓	✓
S16	621	✓	✓
S17	Unidentified	✓	✓
S18	Unidentified		
S19	904	✓	✓
S20	77	✓	✓
S21	Unidentified	✓	✓
S22	496	✓	✓
S23	77	✓	✓
S24	Unidentified	✓	✓
S25	27	✓	✓
S26	162	✓	✓
S27	94	✓	✓
S28	Unidentified	✓	✓
S29	28	✓	✓
S30	77	✓	✓
S31	Unidentified	✓	✓
S32	208	✓	✓
S33	27	✓	✓
S34	Unidentified	✓	✓
S35	828	✓	✓
S36	120	✓	✓
S37	Unidentified		
S38	31	✓	✓
S39	Unidentified	✓	✓
S40	Unidentified	✓	✓
S41	886	✓	✓
S42	31	✓	✓
S43	94	✓	✓
S44	4	✓	✓
S45	621	✓	✓
S46	24	✓	✓
S47	210	✓	✓
S48	212	✓	✓
S49	Unidentified	✓	✓
S50	27	✓	✓
S51	Unidentified	✓	✓
S52		✓	✓
S53		✓	✓

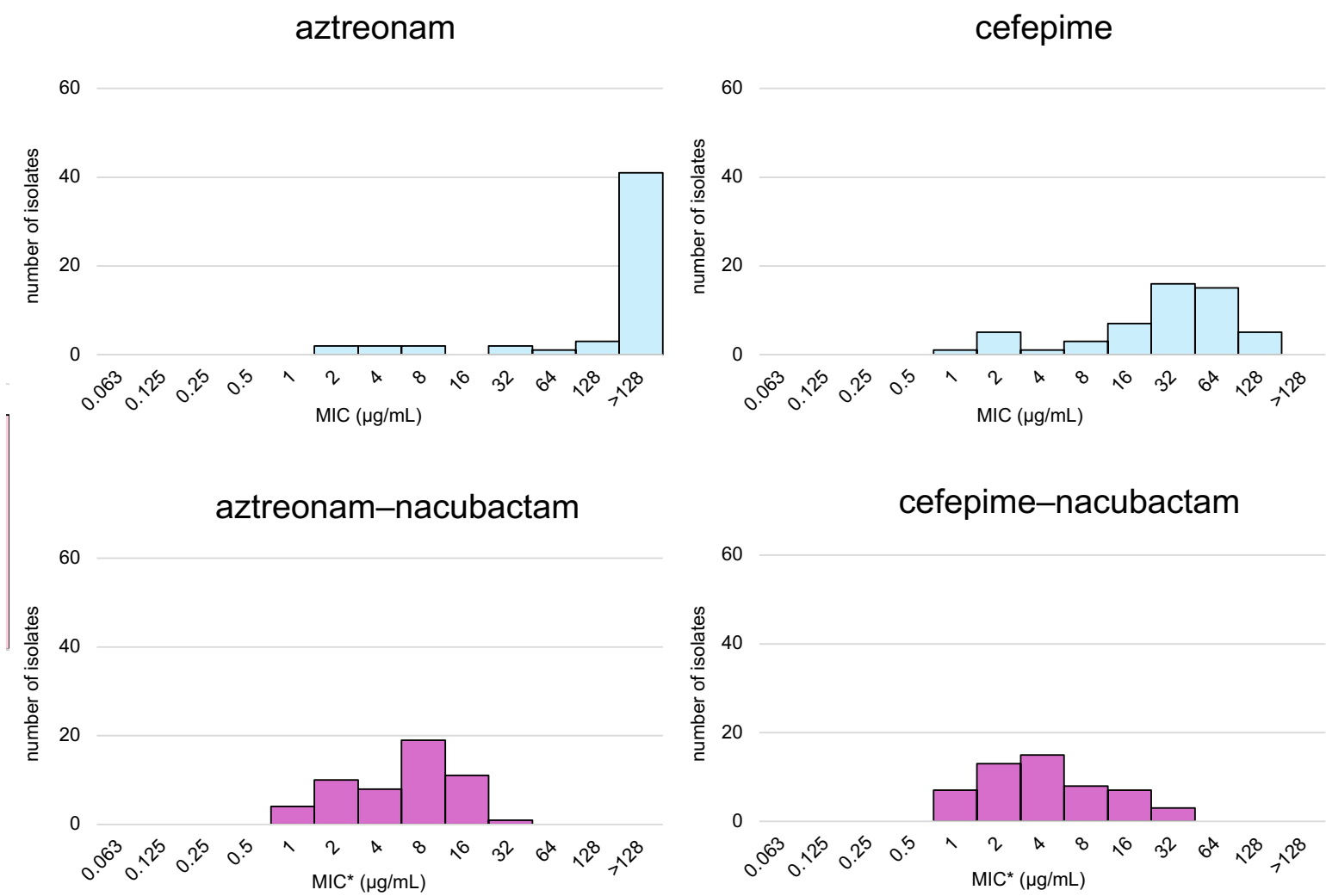


Figure 1. Distribution of MIC values for aztreonam, cefepime alone, and their respective combinations.

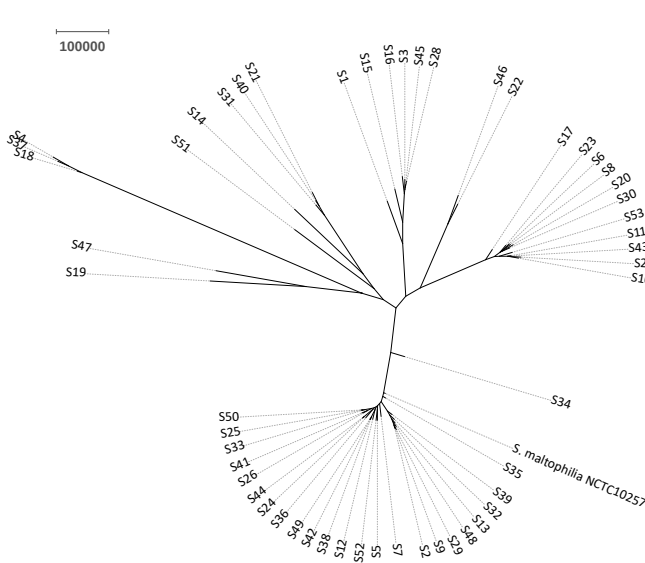


Figure 2. Phylogenetic tree of isolates based on core genome SNP analysis.

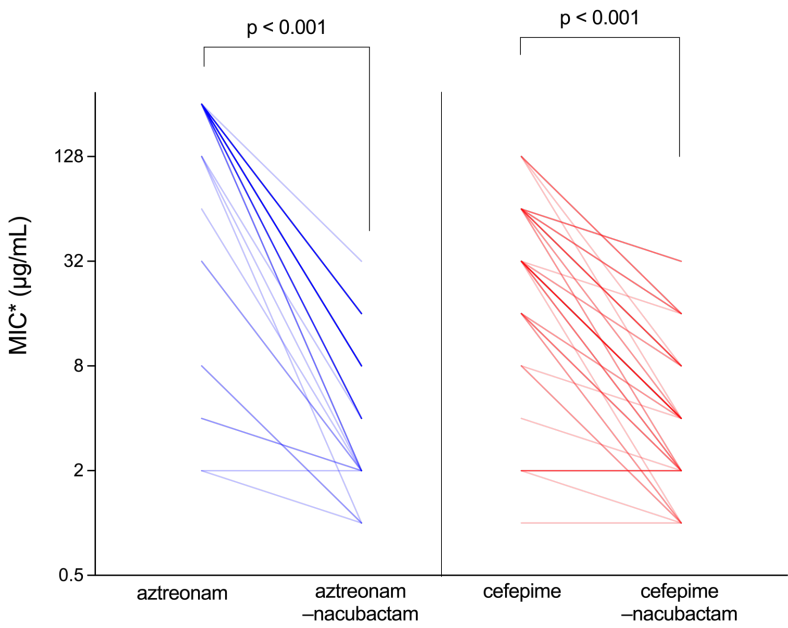


Figure 3. The effect of nacubactam combination on MIC reduction.

Table 1. Sequence types and presence of *bla*<sub>L1</sub> and *bla*<sub>L2</sub> genes in the isolates

Conclusion

- ✓ ATM-NAC and FEP-NAC showed substantial in vitro activity against *S. maltophilia* bacteremia isolates.
- ✓ Given the desire to preserve RESERVE agents like ATM, FEP-NAC—using a WATCH category drug—may represent a promising alternative, warranting further pharmacokinetic, pharmacodynamic, and in vivo evaluation.