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In vitro activity of Meropenem-Pilabactam and comparators against Carbapenem-resistant *Acinetobacter* clinical Isolates: Implications for Low- and Middle-Income Countries (LMIC)

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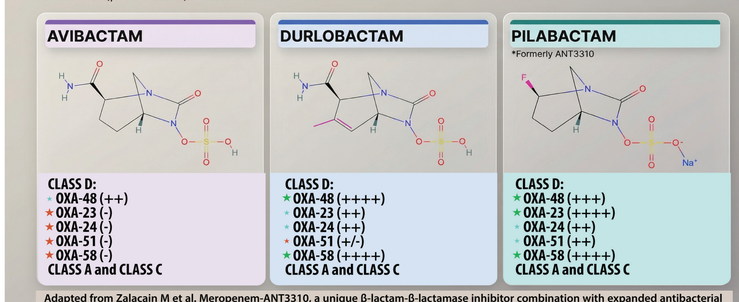
Background

Carbapenem-resistant *Acinetobacter* (CRA) continues to surge globally and is endemic in Latin America and other LMICs. In Argentina, CRA exceeds 90%. CRA is largely driven by class D carbapenemases, mainly bla_{OXA-23}, $bla_{OXA-24/40}$ and bla_{OXA-58}. Pilabactam (formerly, Pilabactam) is a next-generation diazabicyclooctane β-lactamase inhibitor being developed in combination with meropenem (MEM) to treat infections caused by carbapenem-resistant Gram-negatives, including OXA-producing CRA. (Figure A)

Fig. A:
STRUCTURAL COMPARISON AND PROFILES OF BDO INHIBITORS
ANT3310 (pilabactam) vs avibactam vs durlobactam



Adapted from Zalacain M et al. Meropenem-ANT3310, a unique β-lactam-β-lactamase inhibitor combination with expanded antibacterial spectrum against Gram-negative pathogens including carbapenem-resistant *Acinetobacter baumannii*. Antimicrob Agents Chemoter. 2024 Mar 6;68 (3):e0112023. doi: 10.1128/aac.01120-23.

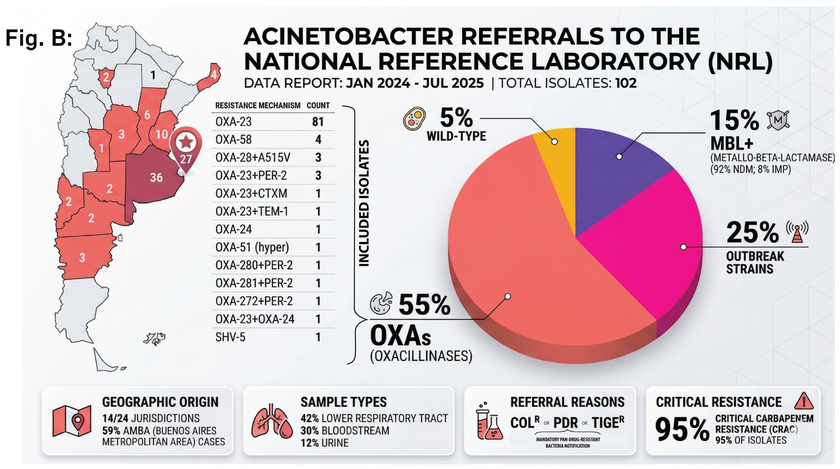
Objective

To evaluate the *in vitro* activity of MEM-Pilabactam and comparators against a contemporary CRA collection.

Methods

- Clinical isolates: 102 clinical isolates, mostly with confirmed extreme/pan-drug resistance. Species: *A. baumannii* (n 97), *A. junii* (1), *A. johnsonii* (1), *A. pittii* (1), *A. ursingii* (1) and *A. bereziniae* (1). Isolate identification was performed using MALDI-TOF. β-lactamase background genotype was determined using PCR/sequencing and/or WGS. (Figure B)
- Reference susceptibility tests followed CLSI. Pilabactam fixed concentration: 8 mg/L; durlobactam: 4 mg/L. Cefiderocol and rifabutin (BV-100) were tested in iron-depleted cation-adjusted Mueller-Hinton broth. A provisional susceptible breakpoint of ≤ 8 mg/L was applied for MEM-Pilabactam and rifabutin; other agents were interpreted per CLSI, EUCAST and/or FDA. Fisher's exact test (two-tailed) was used for comparisons.

Fig. B:



Results

MEM alone showed MIC50 and MIC90 of 128 and 512 mg/L; with Pilabactam the MIC50/90 decreased to 1 and 4 mg/L, respectively (Figure 1 and Figure 2). MEM- Pilabactam was the most active agent (99% susceptible) and did not differ significantly from sulbactam-durlobactam or rifabutin. MEM-Pilabactam outperformed tigecycline, colistin, cefiderocol, amikacin and sulbactam (Figure 3).

Figure 1. MIC summary for novel agents against carbapenem-resistant *Acinetobacter*

Antimicrobial agent	MIC50 (mg/L)	MIC90 (mg/L)	Range (mg/L)
MEM	128	512	0.5* - 512
MEM-Pilabactam	1	4	<=0.03 - 256
SUL	8	32	1 - 256
SUL-DURLO	1	4	<=0.12 - 256
RIFABUTIN	0.25	4	<=0.008 - >16
CEFIDEROCOL	1	16	0.12 - >64

MEM: meropenem. SUL: sulbactam. DURLO: durlobactam. Fixed inhibitor concentrations: Pilabactam 8 mg/L; durlobactam 4 mg/L.
*Two *non-baumannii* isolates carrying acquired bla_{OXAs} were phenotypically susceptible to MEM.

Figure 2. Cumulative MIC distributions agaist carbapenem-resistant *Acinetobacter*

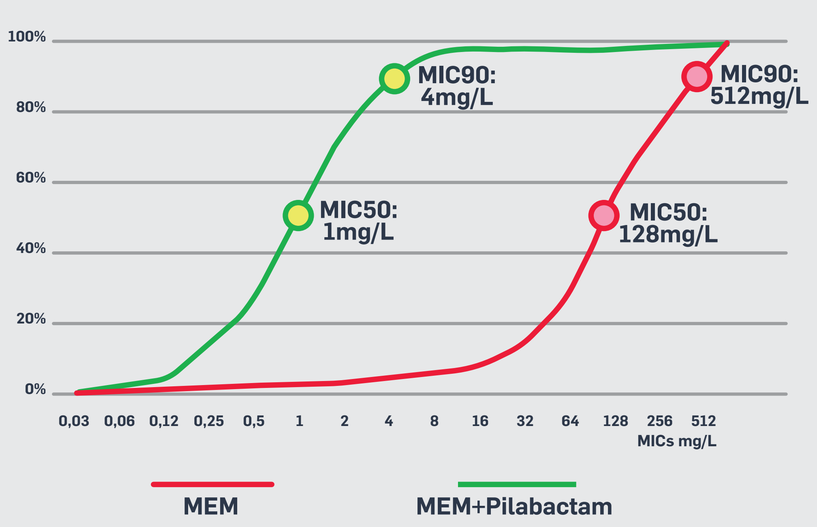
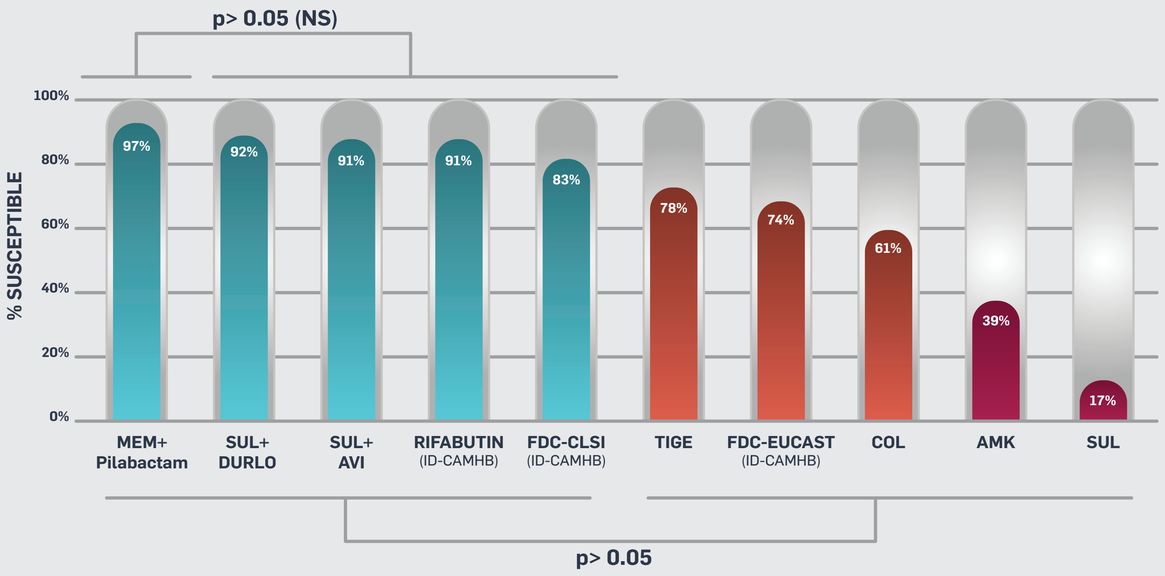


Figure 3. Susceptibility of carbapenem-resistant *Acinetobacter* to MEM-Pilabactam and comparators.



MEM: Menopenem. SUL: Sulbactam. DURLO: Durlobactam. AVI: Avibactam. FDC: Cefiderocol. TIGE: Tigecycline. COL: Colistin. AMK: Amikacin. ID-CAMHB: Iron-depleted cation adjusted Mueller Hinton broth. NS: Non-significant difference.

Conclusions

Pilabactam restored MEM activity against a difficult, referral-based CRA panel, dominated by OXA-23 endemic background and representing isolates harder to treat than routine clinical populations. Activity was comparable to sulbactam-durlobactam and superior to cefiderocol.
These results position MEM-Pilabactam as a reliable option for LMICs, restoring MEM utility against OXA-mediated CRA in settings with constrained access to new antibiotics.

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