

# Meropenem-pilabactam(ANT3310): a novel agent targeting serine carbapenemase-producing Enterobacterales

M. Echegorry<sup>1</sup>, L. Maccari<sup>1</sup>, P. Ceriana<sup>1</sup>, M Rapoport<sup>1</sup>, C. Lucero<sup>1</sup>, MA Menocal<sup>1</sup>, A. Corso<sup>1</sup>, F. Pasteran<sup>1</sup>

<sup>1</sup>Servicio Antimicrobianos, Laboratorio Nacional de Referencia en Antimicrobianos INEI-ANLIS Dr. Carlos G. Malbrán, Buenos Aires, Argentina

www.antimicrobianos.com.ar

Contact: marianoechegorry@gmail.com; fpasteran@gmail.com

## INTRODUCTION

Carbapenemase-producing Enterobacterales (CPE) represent an increasing global public health threat, limiting available therapeutic options. Serine carbapenemases (SCP) are among the main mechanisms driving carbapenem resistance. Current treatment protocols primarily rely on agents like ceftazidime-avibactam (CZA) and imipenem-relebactam (IMR). Pilabactam (PIL- previously ANT3310), a next generation diazabicyclooctane SCP inhibitor, is being developed in combination with meropenem for the treatment of severe infections caused by Gram-negative pathogens in hospitalized patients. This study evaluates the in vitro activity of MEM-ANT3310 against a diverse collection of SCPE clinical isolates.

## MATERIALS AND METHODS

### 407 Enterobacterales and 4 ATCC strains

Clinical isolates from a National Prevalence Survey

*K. pneumoniae* 700603  
*K. pneumoniae* BAA1705  
*P. aeruginosa* 27853  
*E. coli* 25922

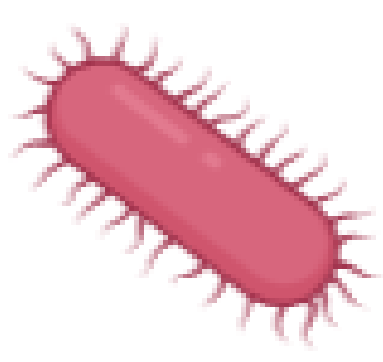


### Carbapenem resistant mechanism

327 blaKPC  
21 blaKPC+blaOXA-163  
59 blaOXA-163

### Species identification (n)

325 *Klebsiella pneumoniae*  
32 *Enterobacter cloacae*  
17 *Escherichia coli*  
12 *Serratia marcescens*  
21 Other species



## RESULTS

- At concentrations of  $\leq 8/8$  mg/L, MEM-PIL inhibited 96.3 % of all SCPE (96.0% KPC; 98.3% OXA-163 and 90.5% KPC plus OXA-163).
- MEM-PIL showed statistically superior activity compared to MEM and traditional therapeutic options (fosfomicin, amikacin, tigecycline and colistin) ( $p < 0.0001$ ).
- No statistically significant differences were found in the performance among MEM-PIL, IMR, and CZA ( $p > 0.05$ ).
- Notably, MEM-PIL remained susceptible in all 3 isolates that were non-susceptible to IMR and/or CZA.

## CONCLUSION

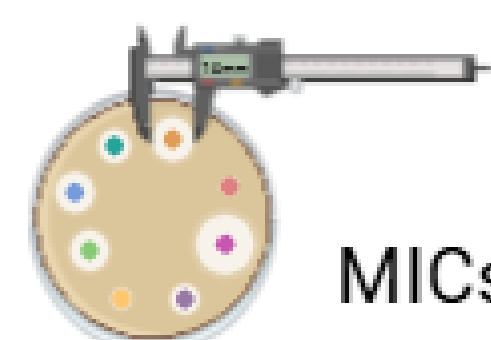
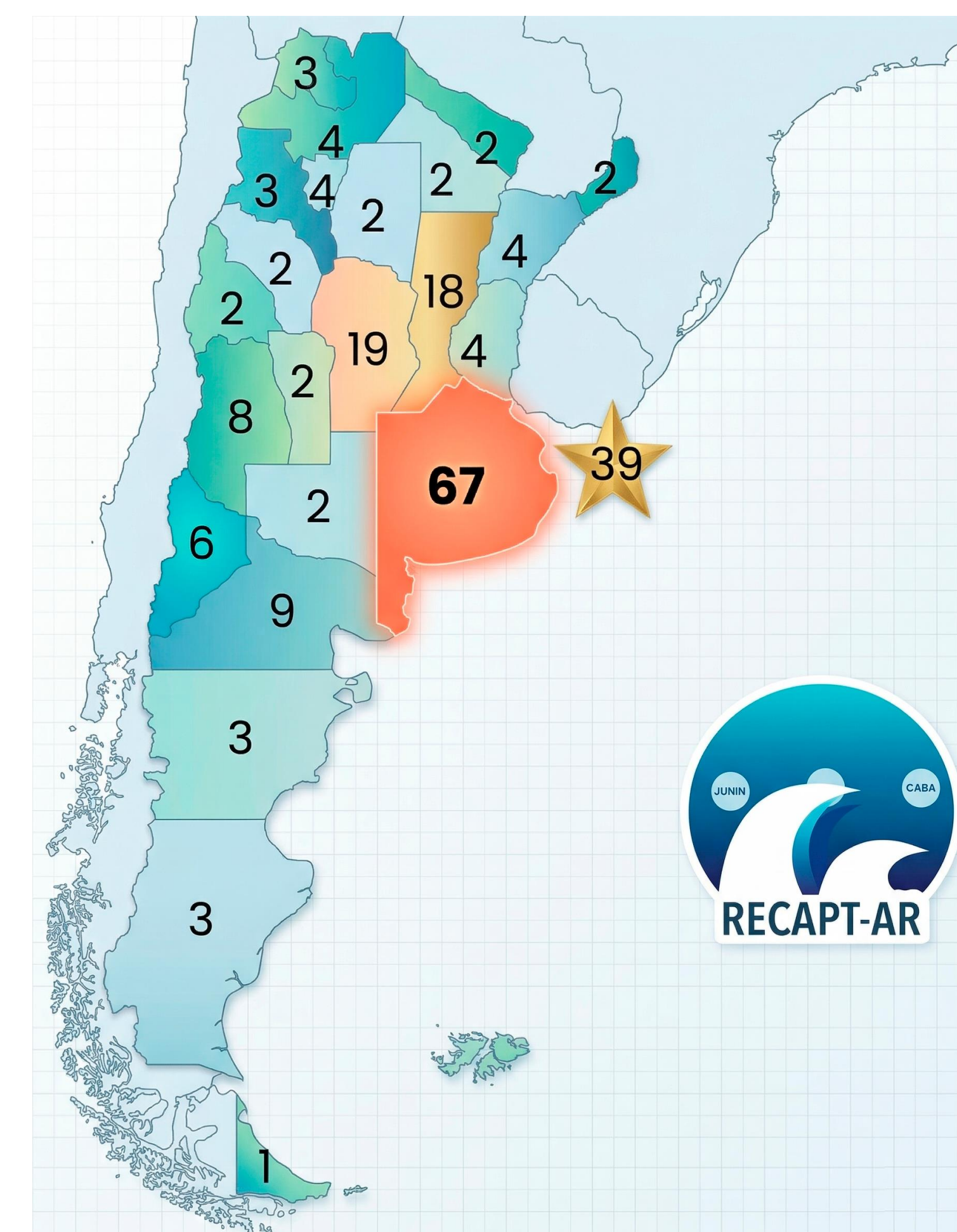
MEM-PIL demonstrated excellent in vitro activity against SCPE, comparable to those of IMR and CZA.

Additionally, its ability to retain activity against isolates non-susceptible to either IMR or CZA suggests a complementary role within the therapeutic armamentarium for SCP.

These findings support MEM-PIL as a promising candidate against SCP in high-burden settings, also in those with emerging resistance or limited access to other  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations.

## AIM

This study evaluates the in vitro activity of MEROPENEM-PILABACTAM (ANT3310) against a diverse collection of SCPE clinical isolates.



### Susceptibility test

MICs were determined by CLSI broth microdilution. ANT3310 was tested at 8 mg/L.

A provisional PK/PDbreakpoint of  $\leq 8/8$  mg/L defined susceptibility for ATM-ANT3310 while comparators antimicrobials were interpreted per CLSI/EUCAST breakpoints.

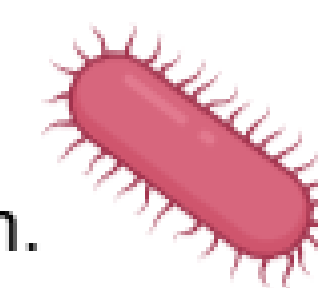


Fig.1 MEM-PIL, CZA and IMR: MIC50, MIC90 and MIC ranges by carbapenemase class

CBP	n	MERO-PILA			IMR			CZA		
		MIC50	MIC90	Range	MIC50	MIC90	Range	MIC50	MIC90	Range
KPC	327	0.12	1	$\leq 0.06 - \geq 128$	0.25	0.5	$\leq 0.12 - 8$	0.5	1	$\leq 0.5 - \geq 32$
OXA	59	0.12	0.5	$\leq 0.06 - 4$	0.5	1	$\leq 0.12 - 4$	2	4	$\leq 0.25 - 64$
KPC + OXA	21	0.25	2	$\leq 0.06 - 32$	0.25	0.5	$\leq 0.12 - 1$	1	2	$\leq 0.25 - 2$
TOTAL	407	0.12	1	$\leq 0.06 - \geq 128$	0.25	1	$\leq 0.12 - 8$	$\leq 0.5$	2	$\leq 0.25 - 64$

CBP: Carbapenemase, MEM-PIL: Meropenem-pilabactam, IMR: Imipenem-relebactam, CZA: Ceftazidime-avibactam. Panel included (n): *K. pneumoniae* (325), *Enterobacter cloacae* (32), *Escherichia coli* (17), *Serratia marcescens* (17), *Morganellaceae* (9), *Klebsiella aerogenes* (7), *Klebsiella oxytoca* (2), *Citrobacter freundii* (2) and *Citrobacter koseri* (1).

## Fig.2 Antimicrobial Susceptibility Rates: Meropenem-pilabactam and Comparator Agents.

CBP	n	% Susceptibility							
		MEM-PIL	IMR		CZA	COL	TIGE	AMK	FOS
		pK/pD	EUCAST	CLSI	CLSI-EUCAST				
KPC	327	96.0	98.5	98.2	97.2	68.8	66.3	66.8	71.1
OXA	59	98.3	95.1	91.8	95.1	78.0	68.3	51.7	71.7
KPC + OXA	21	90.5	100	100	100	31.6	83.3	65.0	65.0
TOTAL	407	96.3	98.3	97.5	97.8	67.4	67.4	64.5	70.9

CBP: Carbapenemase, MEM-PIL: Meropenem-pilabactam, IMR: Imipenem-relebactam, CZA: Ceftazidime-avibactam, COL: Colistin, TIGE: Tigecycline, AMK: Amikacin, FOS: Fosfomicin. Legend: ■ >90% Susceptibility ■ <60% Susceptibility

## Fig.3 MER-PIL MIC Distribution for SCPE

