

In vitro Activity of Zosurabalpin and Comparator Agents Tested Against *Acinetobacter baumannii-calcoaceticus* Complex Isolates From China

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Background

- Zosurabalpin (RG6006) is a first-in-class, novel tethered macrocyclic peptide that prevents intracellular transport of lipopolysaccharide by inhibition of the LptB₂FGC complex.
- Currently zosurabalpin is under clinical development for the treatment of difficult-to-treat *Acinetobacter baumannii-calcoaceticus* complex (ABC) infections including those caused by carbapenem-resistant ABC (CRABC) isolates.
- This study evaluated the *in vitro* antimicrobial activity of zosurabalpin against 100 ABC bacterial isolates collected from two (2) Chinese hospitals, using Clinical and Laboratory Standards Institute (CLSI) reference susceptibility testing methods.

Methods

- Bacterial isolates were collected from patients with documented infections from two (2) Chinese hospitals during 2024; bacterial species were identified as ABC complex using DNA sequencing.
- Susceptibility testing was performed by the CLSI reference broth microdilution method and CLSI, FDA, and EUCAST breakpoint criteria were applied for comparator agents (*n*=6; cefiderocol, amikacin, colistin, imipenem, meropenem, and piperacillin-tazobactam).
- Zosurabalpin was tested in cation-adjusted Mueller-Hinton broth (CAMHB) and CAMHB supplemented with 10% or 20% heat-inactivated horse serum (HoS).
 - Zosurabalpin CAMHB MIC endpoints were determined at substantial reduction (SR) and complete inhibition of growth (100%).
 - Zosurabalpin CAMHB with HoS MIC endpoints were determined at complete inhibition of growth (100%).
- Cefiderocol testing was performed in iron-depleted CAMHB while remaining comparator agents were tested in standard CAMHB.

Results

- Zosurabalpin displayed potent activity against this set of ABC isolates from China, with MIC_{50/90} values of 0.25/0.5 mg/L when tested in CAMHB supplemented with 10% or 20% HoS and when tested in CAMHB without serum and read at SR (Table 1).
- All ABC isolates (100%; 100/100) were inhibited at 1 mg/L when tested in CAMHB with HoS and 98% of isolates (98/100) tested in CAMHB and read at SR (Figure 1).
- The zosurabalpin MIC_{50/90} values obtained in CAMHB were 1/>32 mg/L when read at 100%.
- Isolates were resistant to comparator antimicrobial agents including amikacin, imipenem, meropenem, and piperacillin-tazobactam (4%–9% susceptible) when CLSI, EUCAST, and FDA breakpoint criteria were applied (Table 1).
- Most isolates (94%; 94/100) demonstrated resistance to both meropenem and imipenem, indicative of a CRABC phenotype.
- Among comparators, colistin (94% susceptible per EUCAST; MIC_{50/90} values of 0.5/1 mg/L) and cefiderocol (94%/99% susceptible per CLSI/FDA; MIC_{50/90} values of 0.25/1 mg/L) comparator agents displayed activity against the majority of this 100-isolate set.

Conclusions

- Zosurabalpin demonstrated potent *in vitro* activity against recent ABC isolates—including CRABC—collected from patients in two Chinese hospitals during 2024.
- Zosurabalpin MIC values read under SR criteria in CAMHB were similar to those read in CAMHB media supplemented with 10% or 20% HoS (MIC_{50/90} 0.25/0.5 mg/L).
- Zosurabalpin may represent a potential option for treatment of infections caused by CRABC and further studies are needed to demonstrate its clinical effectiveness.

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Figure 1. Cumulative MIC distribution of zosurabalpin and comparator agents tested against 100 *Acinetobacter baumannii-calcoaceticus* complex (ABC) isolates from two Chinese hospitals

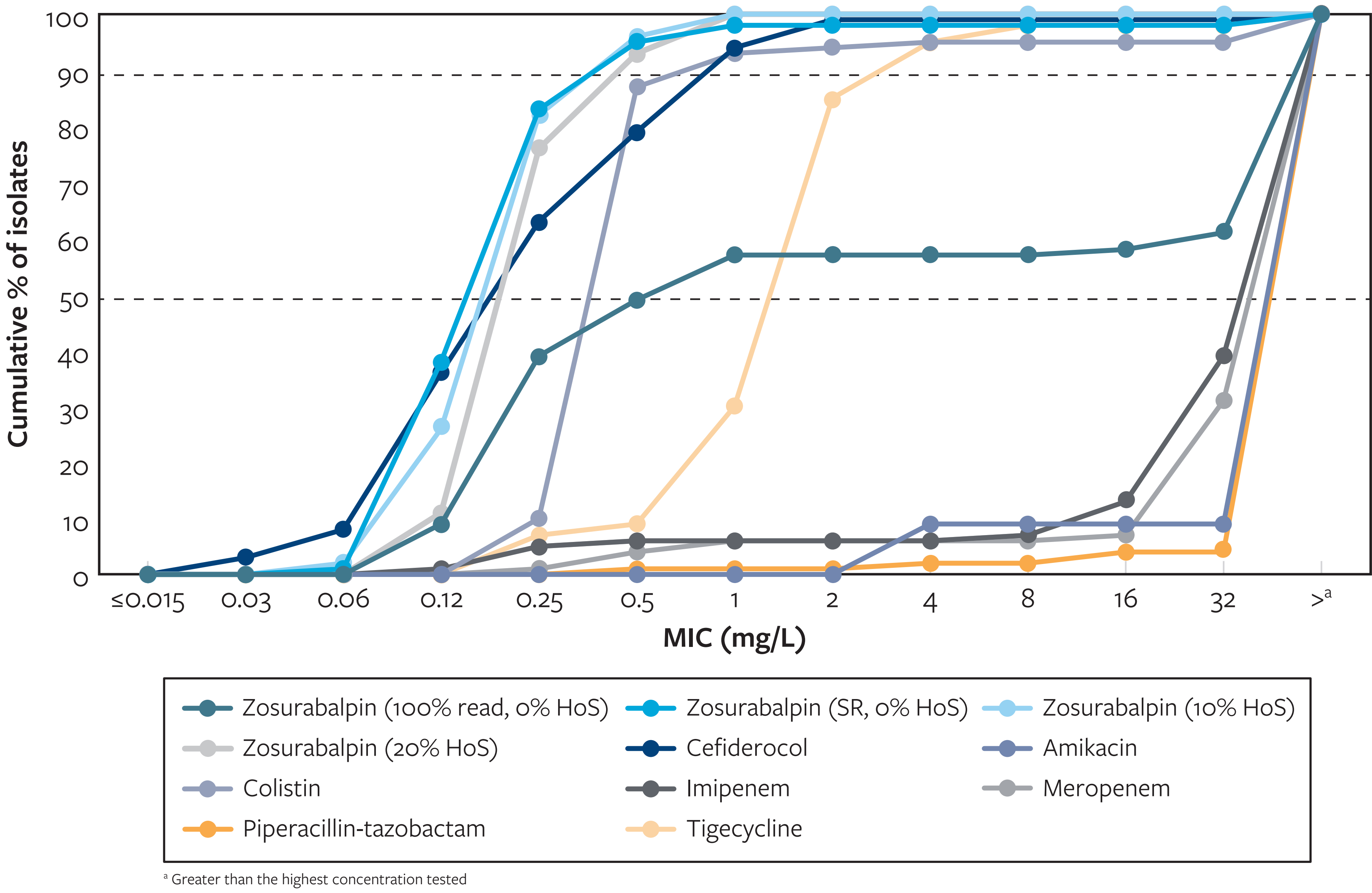


Table 1. Activity of zosurabalpin and comparator agents tested against 100 *Acinetobacter baumannii-calcoaceticus* complex (ABC) isolates from two Chinese hospitals

Antimicrobial Agent	Concentration (mg/L)											% Susceptible ^a			
	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>	MIC ₅₀	MIC ₉₀	CLSI	FDA
Zosurabalpin (100% read, 0% HoS)	0	9	30	10	8	0	0	0	1	3	39	1	>32		
	0.0%	9.0%	39.0%	49.0%	57.0%	57.0%	57.0%	57.0%	58.0%	61.0%	100.0%				
Zosurabalpin (SR, 0% HoS)	1	37	45	12	3	0	0	0	0	0	2	0.25	0.5		
	1.0%	38.0%	83.0%	95.0%	98.0%	98.0%	98.0%	98.0%	98.0%	98.0%	100.0%				
Zosurabalpin (10% HoS)	2	24	56	14	4							0.25	0.5		
	2.0%	26.0%	82.0%	96.0%	100.0%										
Zosurabalpin (20% HoS)	0	11	65	17	7							0.25	0.5		
	0.0%	11.0%	76.0%	93.0%	100.0%										
Cefiderocol	8	28	27	16	15	5	0	0	0	0	1	0.25	1	99.0	94.0
	8.0%	36.0%	63.0%	79.0%	94.0%	99.0%	99.0%	99.0%	99.0%	99.0%	100.0%				
Amikacin ^c						0	9	0			91	>8	>8		
						0.0%	9.0%	9.0%			100.0%				
Colistin		0	10	77	6	1	1	0			5	0.5	1		94.0
		0.0%	10.0%	87.0%	93.0%	94.0%	95.0%	95.0%			100.0%				
Imipenem	0	1	4	1	0	0	0	1	6	26	61	>32	>32	6.0	6.0
	0.0%	1.0%	5.0%	6.0%	6.0%	6.0%	6.0%	7.0%	13.0%	39.0%	100.0%				
Meropenem	0	1	3	2	0	0	0	0	1	24	69	>32	>32	6.0	6.0 ^d
	0.0%	1.0%	4.0%	6.0%	6.0%	6.0%	6.0%	6.0%	7.0%	31.0%	100.0%				
Piperacillin-tazobactam			0	1	0	0	1	0	2	0	96	>128	>128	4.0	4.0
			0.0%	1.0%	1.0%	1.0%	2.0%	2.0%	4.0%	4.0%	100.0%				
Tigecycline		0	7	2	21	55	10	3			2	2	4		
		0.0%	7.0%	9.0%	30.0%	85.0%	95.0%	98.0%			100.0%				

^a Criteria as published by CLSI (2024), EUCAST (2024), and US FDA (2024).
^b For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.
^c Amikacin was tested below CLSI and FDA breakpoint criteria.
^d Using meningitis and non-meningitis breakpoints.
Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; HoS, heat-inactivated horse serum; MIC, minimum inhibitory concentration (mg/L); SR, substantial reduction; US, United States.