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Antimicrobial Spectrum of Plazomicin and Other Aminoglycosides against Multidrug-Resistant and Carbapenem-Resistant Enterobacterales When Applying New Breakpoints

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Introduction

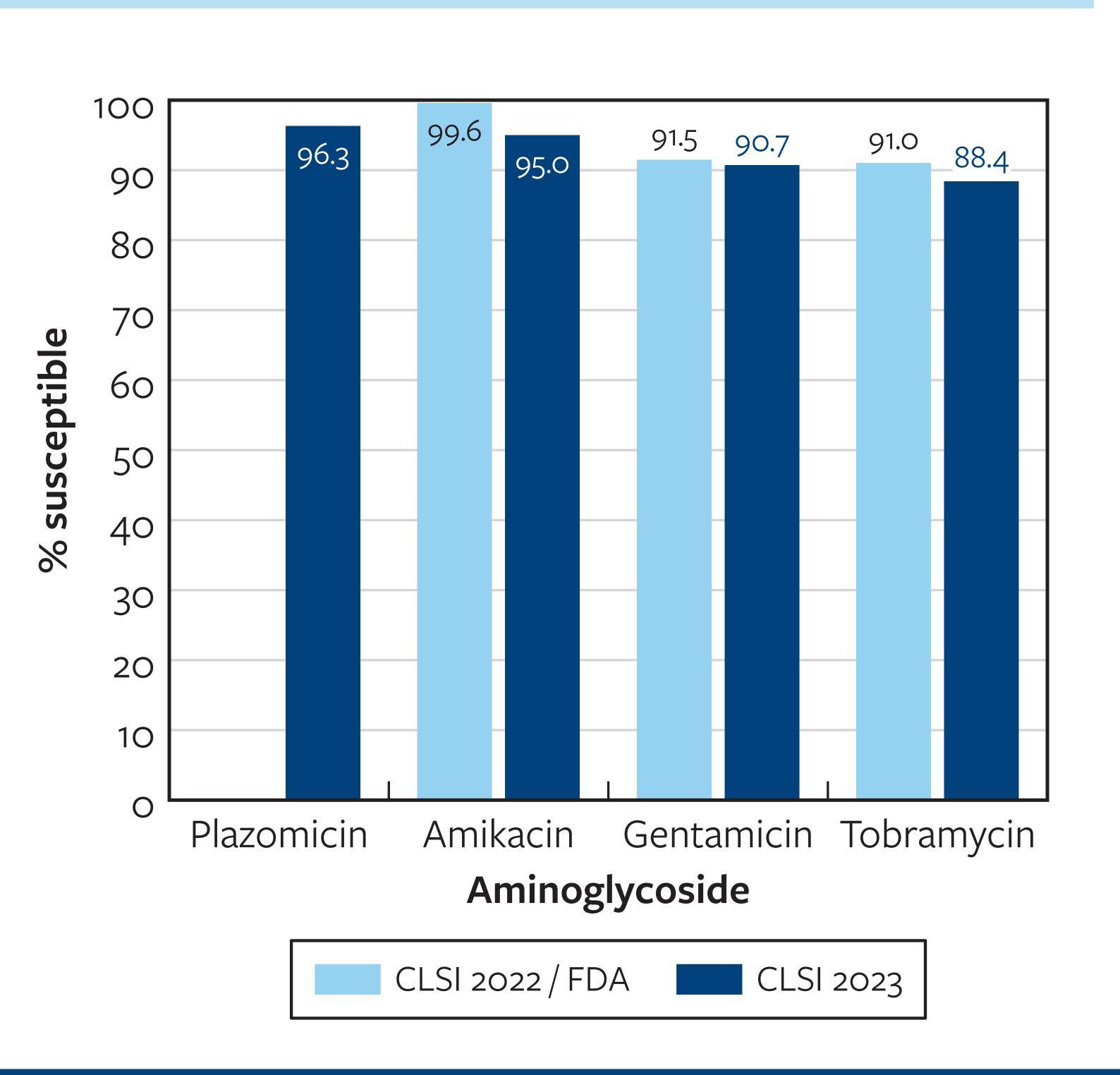
- In March 2023, the Clinical and Laboratory Standards Institute (CLSI) lowered the Enterobacterales susceptible/resistant breakpoints for amikacin from $\leq 16/\geq 64$ mg/L to $\leq 4/\geq 16$ mg/L and gentamicin and tobramycin from $\leq 4/\geq 16$ mg/L to $\leq 2/\geq 8$ mg/L.
- Aminoglycosides are frequently used to treat infections caused by multidrugresistant (MDR) and carbapenem-resistant Enterobacterales (CRE).
- We evaluated the activity of plazomicin and the impact of CLSI breakpoint changes on the susceptibility rates of Enterobacterales collected from US medical centers.

Methods

- 5,725 Enterobacterales isolates were consecutively collected (1/patient) from 36 US medical centers in 2020–2022.
- Isolates were susceptibility tested by broth microdilution against amikacin, gentamicin, tobramycin, and plazomicin.
- Susceptibility rates were calculated using both the 2022 CLSI/USFDA breakpoints and the recently revised (2023) CLSI breakpoints.
- Aminoglycoside-nonsusceptible isolates were screened for genes encoding aminoglycoside-modifying enzymes (AMEs) and 16S rRNA methyltransferases (16RMT).

Results

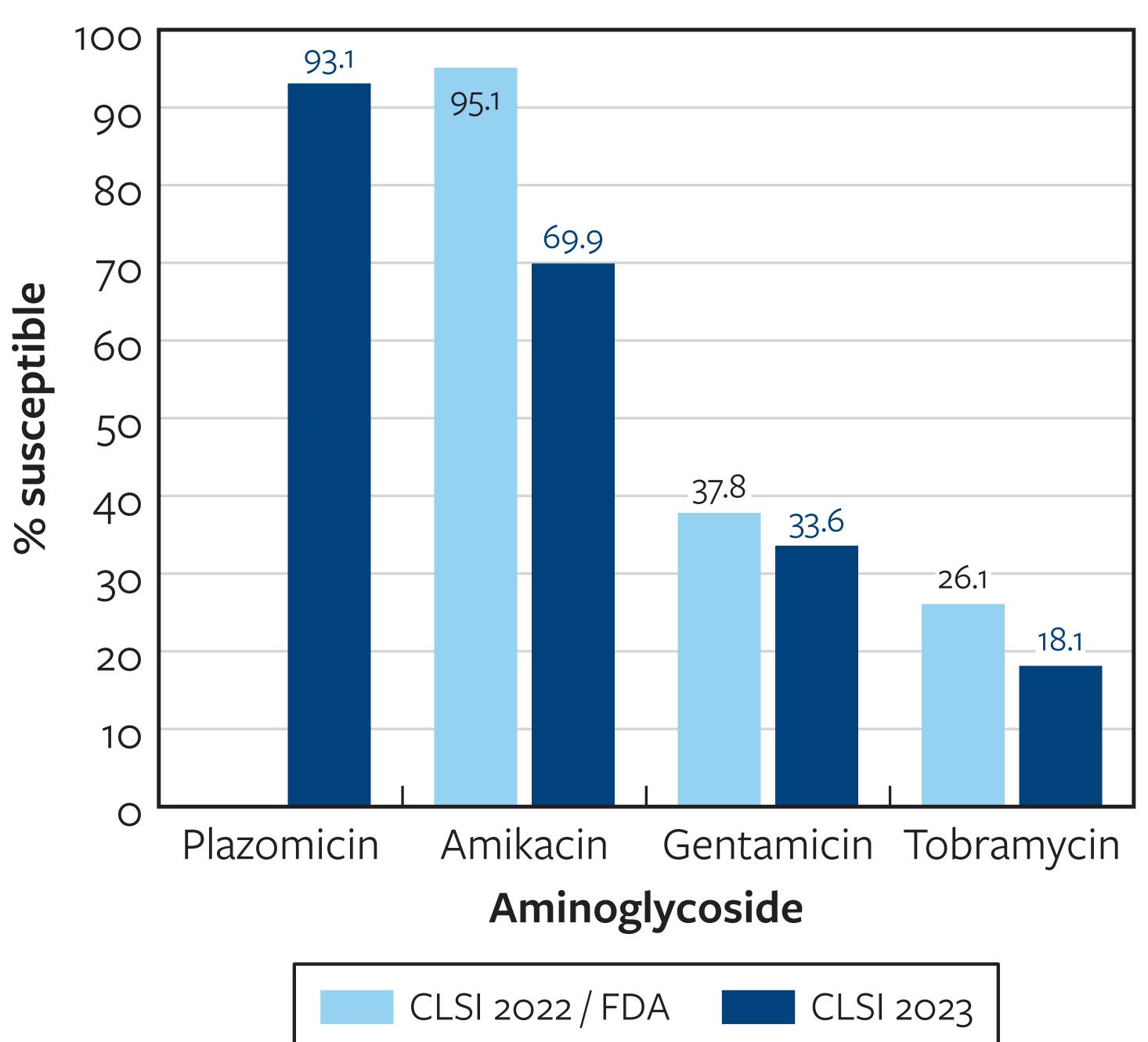
- Plazomicin was active against 96.3% of isolates and retained potent activity against MDR (93.1%S) and CRE (92.1%S) isolates (Table 1 and 2 and Figure 1 to 3).
- The highest variations in susceptibility rates due to breakpoint changes were observed with amikacin, especially among MDR (95.1%S to 69.9%S) and CRE (77.8%S to 61.9%S; Table 1 and 2 and Figure 1 to 3).
- Against all Enterobacterales, amikacin susceptibility rates decreased from 99.6%S to 95.0%S; susceptibility to gentamicin and tobramycin decreased 0.8% and 2.6%, respectively (Table 1 and Figure 1).
- Gentamicin and tobramycin showed limited activity against MDR and CRE with both 2022 and 2023 breakpoints (Table 1 and 2 and Figure 2 and 3).
- AME-encoding genes were observed in 474 (8.3% of isolates) and 16RMT was found in 7 isolates (0.1%).
- Plazomicin was active against 97.3% of AME producers (Tables 1 and 2).



	% Susceptible / % Resistant							
	All Enterobacterales (n=5,725)		MDR Enterobacterales (n=452)		CRE (n=63)		AME Producers (n=474)	
Aminoglycoside	CLSI 2022	CLSI 2023	CLSI 2022	CLSI 2023	CLSI 2022	CLSI 2023	CLSI 2022	CLSI 2023
Plazomicin		96.3/0.9		93.1/3.5		92.1/6.3		97.3/1.7
Amikacin	99.6/0.2	95.0/1.3	95.1/2.4	69.9/13.5	77.8/9.5	61.9/27.0	94.9/2.1	72.8/10.8
Gentamicin	91.5/7.8	90.7/8.5	37.8/57.1	33.6/62.2	68.3/25.4	57.1/31.7	12.9/86.1	11.4/87.
Tobramycin	91.0/5.9	88.4/9.0	26.1/57.1	18.1/73.9	42.9/52.4	39.7/57.1	15.0/63.9	2.1/85.0

Figure 1. Susceptibility rates for the Enterobacterales collection





Antimicrobial ag Plazomicin Amikacin Gentamicin Tobramycin Aztreonam Ceftriaxone Ceftazidime Cefepime Piperacillin-tazoba mipenem Meropenem Levofloxacin TMP-SMX

-igecycline ^b DA breakpoints were applied

crobial susceptibility of Enterobacterales and resistant subsets from US medical centers (2020–2022)									
	% Susceptible per 2023 CLSI criteria (no. of isolates)								
gent	Enterobacterales (5,725)	MDR (452)	CRE (63)	AME Produ					
	96.3 ^a	93.1 ^a	92.1 ^a	97.					
	95.0	69.9	61.9	72					
	90.7	33.6	57.1	11					
	88.4	18.1	39.7	2.					
	85.6	12.6	4.8	34					
	82.7	4.9	3.2	31					
	86.1	11.1	7.9	35					
	88.2	15.5	9.5	33					
actam	88.3	33.0	4.8	60					
	92.9 ^a	82.7 ^a	4.8 ^a	92.					
	98.8	85.4	1.6	93					
	81.6	11.7	22.2	32					

27.0

93.4

Table 2. Antimicrobial susceptibility of Enterobacterales and resistant subsets from US medical centers (2020–2022)

Il Enterobacterales species were included in the analysis, but CLSI excludes Morganella, Proteus, and Providencia species

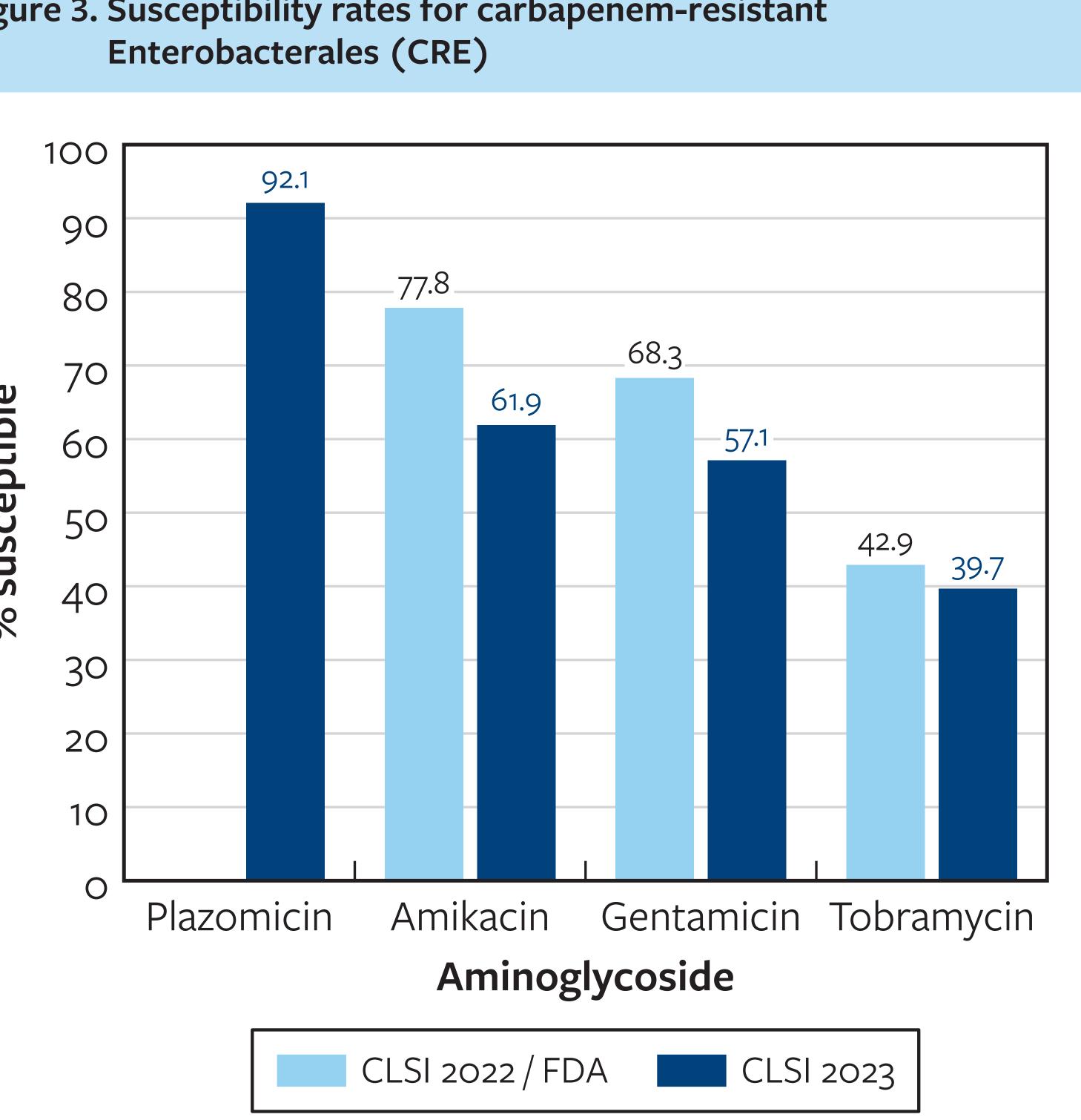
79.9

97.5

Figure 3. Susceptibility rates for carbapenem-resistant Enterobacterales (CRE)

34.9

95.2



ucers (474)

- 5.9

- 32.1
- 19.8
- 95.8

Conclusions

- Amikacin's spectrum of activity against CRE and MDR Enterobacterales was drastically reduced when interpretative criteria based on PK/PD parameters currently used to establish breakpoints to other antimicrobials were applied.
- Plazomicin is markedly more active than amikacin, gentamicin, or tobramycin against CRE and MDR Enterobacterales causing infections in US medical centers.
- Among a wide spectrum of classes of agents tested, plazomicin is the most active agent against AME-producing Enterobacterales isolates causing infections in US medical centers.

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References

CLSI. 2023. M100Ed33. Performance standards for antimicrobial susceptibility testing: 33rd informational supplement. Clinical and Laboratory Standards Institute, Wayne, PA.

Magiorakos AP, Srinivasan A, Carey RB, et al. 2012. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 18:268-281.

Sader HS, Mendes RE, Kimbrough JH, Kantro V, Castanheira M. impact of the recent Clinical and Laboratory Standards Institute breakpoint changes on the antimicrobial spectrum of aminoglycosides and the activity of plazomicin against multidrugresistant and carbapenem-resistant Enterobacterales from United States medical centers. Open Forum Infect Dis. 2023;10(2):ofad058.

US-FDA. Antibacterial susceptibility test interpretive criteria. 2022. https://www .fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive -criteria. Accessed January 2023.

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