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New quinolones, oxazolidones, and a chimera of both

IN VITRO ACTIVITY OF TEDIZOLID AGAINST STAPHYLOCOCCUS AUREUS AND LINEZOLID-RESISTANT GRAM-POSITIVE COCCI

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Objectives To evaluate the *in-vitro* antimicrobial activities of tedizolid against *Staphylococcus aureus* and linezolid-resistant Gram-positive cocci isolates.

Methods The non-duplicated 100 methicillin-resistant *Staphylococcus aureus* (MRSA) isolates, 100 methicillin-sensitive *Staphylococcus aureus* (MSSA), and 43 coagulase-negative staphylococci (CNS) and 17 enterococci isolates resistant to linezolid were collected from 14 teaching hospitals across China from January 2009 to August 2013. The levels of minimal inhibitory concentration (MIC) of tedizolid, linezolid and other comparators were determined by broth microdilution method. The data were analyzed by WHONET 5.6 software. Domain V of the 23S rRNA mutations and the *cfr* gene were detected by PCR combined nucleotide sequence.

Results The MIC₉₀ of 200S. *aureus* to tedizolid (0.5 mg/L) was 4 fold lower than linezolid (2 mg/L). 88.4% (38/43) linezolid-resistant CNS harbored the multi-drug resistant gene *cfr* and 60.5% (26/43) had 23S rRNA mutation G2576T. Based on the MIC₉₀ values, the potency of tedizolid against CNS (MIC₉₀ = 4 mg/L) was > 64-fold greater than that of linezolid (MIC₉₀ > 256 mg/L). Tedizolid retained activity against all of the 43 linezolid-resistant staphylococci tested, including *cfr*-positive or having G2576T mutations in 23S rRNA isolates with elevated linezolid MICs (16 to > 256 mg/L). Of the linezolid-resistant staphylococci isolates, 100% and 77% were inhibited by tedizolid both at ≤ 4 mg/L and ≤ 2 mg/L, respectively. Tedizolid demonstrated high antimicrobial activity to all 17 linezolid-resistant enterococci. None of the enterococci strains carried the *cfr* gene or had 23S rRNA mutation G2576T. The MIC₉₀ of enterococci to tedizolid (1 mg/L) were 16 fold lower than linezolid (16 mg/L).

Conclusions Tedizolid was highly potent against *S. aureus* and linezolid-resistant Gram-positive pathogens, including *cfr*-positive strains.

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