Antimicrobial Activity of TD-1607 Tested against Contemporary (2010-2012) Methicillin-Resistant Staphylococcus aureus (MRSA) Strains

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INTRODUCTION

Staphylococcus aureus continues to be a major cause of both community- and healthcare-associated infections, including skin and skin structure infections (SSSI), bacteremia, endocarditis and pneumonia. The prevalence of nosocomial infections caused by methicillin-resistant S. aureus (MRSA) has increased in recent years throughout the United States and many other regions of the world. In 2010-2012, MRSA accounted for 39% of SSSI, 16% of bacteremia, 20% of community-acquired pneumonia (CAP) (USDHHS, 2014) and 16% of healthcare-associated pneumonia (HAP) (Spellberg et al., 2014).

MATERIALS AND METHODS

Bacterial isolates

A total of 1,026 MRSA isolates collected through the SENTRY Antimicrobial Surveillance Program network, including 512 isolates from the USA, 312 from Europe and 202 from Latin America, were selected for this investigation. The isolates were collected in 2010-2012 (mostly 2012) from surveillance networks, including the first 500 isolates from the United States, 199 from the European Union, and 127 from Mexico, Canada and Latin America. Clinical isolates were categorized as susceptible with CLSI and EUCAST criteria, respectively.

Susceptibility testing

Susceptibility testing was performed by reference broth microdilution methods (CLSI M07-A9; 2012) using frozen-form (CN) panels prepared by JMI Laboratories with cation-adjusted Mueller-Hinton broth. For TD-1607 (lot #AC002821), a stock solution was prepared at 1037.5 µg/mL, by adding sterile water to starch phosphate buffer at pH 6.0 (±0.1 pH). CLSI (M07-A10; 2012) and EUCAST (version 4.0; 2014) interpretive criteria were applied for comparator agents.

RESULTS

TD-1607 showed potent in vitro activity against MRSA strains. TD-1607 MIC values ranged from 0.12 to 5.0 µg/mL, with MIC50 and MIC90 of 0.35 µg/mL (Table 1 and Figure 1).

TD-1607 MIC values were slightly lower in the USA and Europe compared to Latin America (MIC50, 0.03 µg/mL and MIC90, 0.06 µg/mL). Against the entire collection of MRSA (1,026 isolates), TD-1607 was 16- to 32-fold more active than daptomycin (MIC50, 0.5 µg/mL; Figure 2), vancomycin (MIC50, 1 µg/mL), teicoplanin (MIC50, 0.5 µg/mL and MIC90, 1 µg/mL), and 32- to 64-fold more active than imipenem and cefotaxime (MIC50, 1 µg/mL and MIC90, 2 µg/mL, for both compounds; Table 2).

All isolates were susceptible to vancomycin (MIC50 and MIC90, 1 µg/mL), daptomycin (MIC50 and MIC90, 0.5 µg/mL) and teicoplanin (MIC50, 1 µg/mL; Table 2). When tested against teicoplanin (MIC50, 0.5 µg/mL; MIC90, 0.5 µg/mL; MIC90, 0.12 µg/mL; Figure 3) and comparator agents, TD-1607 MIC values were slightly higher (MIC50, 0.03 µg/mL; Table 2). Resistance rates to comparator agents were generally higher among MRSA isolates from Latin America compared to USA and Europe (data not shown).

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REFERENCES