Antimicrobial Activity of PZ-601 (SMP-601) Tested Against Selected Wildtype and Resistant Collections of Targeted Species (USA and Europe)

Ronald N. Jones, Jennifer M. Streit, Douglas J. Bledenbach, Thomas R. Frische, Helio S. Sader; JMI Laboratories, North Liberty, IA, USA

Abstract

E-268

Abstract

E-268

Introduction

The emergence of bacterial resistance against many commonly used antimicrobials has created a serious therapeutic concern and resulted in increased utilization of carbapenems for Gram-negative pathogens and vancomycin, daptomycin and linezolid for Gram-positive infecting organisms. The increased resistance has also created a need to produce new antimicrobial options especially agents stable to various emerging β-lactamases (extended spectrum β-lactamases; ESBL). PZ-601 (formerly SMP-601) is a novel parenteral carbapenem with a broad spectrum of activity against methillin-resistant Staphylococcus aureus (MRSA), some vancomycin-resistant enterococci (VRE) and many species of Enterobacteriaceae and many species of Entrobacteriaceae (ESBL). PZ-601 has a history of increased activity against MRSA and enterococci compared to existing carbapenems.

The purpose of this study was to establish the PZ-601 MIC distribution for wildtype (WT) S. aureus, Escherichia coli, Klebsiella pneumoniae, and Klebsiella oxytoca strains from both North America (United States; USA) and Europe, as well as potency against specific PZ-601-resistant subsets.

Materials and Methods

Bacterial isolates: A total of 1560 non-duplicate strains were selected to represent a susceptible, WT set of isolates to produce a MIC distribution for PZ-601. Strains were identified as not having unusual resistance patterns to comparable carbapenem agents such as imipenem (e.g., metabolite β-lactamases, open carbapenemases, hyper-producing Amp-C enzymes associated with porin alterations, etc.). The WT isolate distribution included MRSA (500), E. coli (500), K. pneumoniae (400), and K. oxytoca (100), with sufficient sample size to assure high confidence (Orndorff ICPD, 2007). The resistance subsets consisted of metals β-lactamase producing Enterobacteriaceae (IMP-, VIM-series),10 serine β-lactamase-producing Enterobacteriaceae (KPC-, SME-, NmcA-type, 20), MRSA exhibiting elevated vancomycin results (VISA, VREVA, and VRSA, 10), staphylococci with linezolid resistance (10), and community-acquired MRSA (CA-MRSA) clone USA300-0114 and variants (10). Isolates originated from Europe and North America and were cultured in 2005-2006.

Susceptibility Test Methods: Isolates were identified by the reference broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI). The MICs were determined using the CLSI broth microdilution method (CLSI M7-A7, Methods for dilution antimicrobial susceptibility testing—sixth edition) (CLSI, 2007) and were interpreted using the guidelines (M100-S17, Methods for dilution antimicrobial susceptibility testing—seventh edition) (CLSI, 2007) and CLSI reference strains (2005-2006) for comparative purposes. Results were determined as susceptible (MIC ≤ 0.12 μg/ml), intermediate (MIC 0.25-1.0 μg/ml), resistant (MIC > 1.0 μg/ml) and resistant to testing (MIC > 32 μg/ml).

Results

PZ-601 MIC distributions for all nine tested organism groups are shown in Table 1. PZ-601 had bimodal MICs of 0.25 and 1 μg/ml with different predominant modes for USA (0.25 μg/ml) and Europe (1 μg/ml). CA-MRSA USA300 strains had PZ-601 MIC results at >32 μg/ml with VISA and VRSA isolates all inhibited at ≤ 0.06 μg/ml (99.4% inhibited at ≤ 0.015 μg/ml). PZ-601 was also active against K. oxytoca (100) 0 0 2 54 23 11 5 3 2 0 0 0 0 against all staphylococci.

References Cited


Clinical and Laboratory Standards Institute. (2007). M100-S17: Performance standards for antimicrobial susceptibility testing. 17th informational supplement. Wayne, PA, CLSI.