**In Vitro Activity of Lactone Ketolide WCK 4873 When Tested Against Contaminant Community-Acquired Bacterial Pneumonias from a Global Surveillance Program**

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**Background:** WCK 4873 is a novel ketolide antibiotic of the lactic acid bees class currently in clinical development for the treatment of community-acquired lower respiratory tract infections (ALRTIs) and extended-spectrum beta-lactamase (ESBL) and metallo-β-lactamase (MβL) Pseudomonas aeruginosa. It has completed single ascending dose (SAD) and multiple ascending dose (MAD) Phase I studies in Europe and intrapulmonary pharmacokinetic study in U.S. WCK 4873 was awarded Qualified Infectious Disease Product (QIDP) status in 2015. In this work, WCK 4873 was tested against CABP clinical isolates from collected in medical centers worldwide as part of the 2014 SENTRY Antimicrobial Surveillance Program (SASP) (50/90). This was the first multi-center multi-national study of the in vitro activity of WCK 4873 and the second global bacterial surveillance report by JMI Laboratories for CABP.

**Methods:** A total of 1,512 contemporary (2014) CABP clinical isolates from the United States, 1,556 from Europe, 567 from Asia-Pacific, and 58 from Latin America, as part of the SENTRY Program, were susceptible (≤0.002) to WCK 4873 and multiple comparator agents by reference broth microdilution methods and interpretive criteria.

**Results:**

**Organism selection and specimen source:** A total of 4,133 non-duplicate isolates were collected prospectively during 2014 from 1,134 medical centers located in 13 countries (UK, US, AU, SP, JP, and AUS). Only clinically significant isolates were included in the study (Table 1). The number of species tested by geographic region is shown in Table 2. All species identification was confirmed by MATRIX-Assisted Laser Desorption Ionization-Time Of Flight Mass Spectrometry (MALDI-TOF MS) (Bruker Daltonics, Billerica, Massachusetts, USA) when unavailable by subtyping.

**Susceptibility testing:** MIC values were determined using CLSI Standard microdilution methods as described in CLSI document M07-A9 (2015). The overall susceptibility testing was performed using broth microdilution panels produced by Micro-ID Cards (Becton Dickinson, Sparks, MD). All isolates were tested for susceptibility to telithromycin, clarithromycin, erythromycin, tetracycline, ampicillin, amoxicillin, ceftriaxone, amoxicillin/clavulanate, amikacin, and gentamicin. In addition, time-of-flight mass spectrometry (TOF MS) using the Bruker MALDI Biotyper was performed on all isolates. Additional subtyping was done using the Bruker Q-TOF microcassette method. Inhibition zone diameter readings were performed using standard CLSI broth microdilution methods as described in CLSI document A27-A3 (2015). A total of 4,133 isolates were analyzed. Table 2 shows a breakdown of testing for CABP.

**Conclusion:** WCK 4873 showed a broad range of activity in vitro against the Candida, bacteria, and viruses suceptible to WCK 4873. This report represents the second global bacterial surveillance report by JMI Laboratories for CABP.

**Abbreviations:** MSSA = methicillin-susceptible Staphylococcus aureus; MRSA = methicillin-resistant Staphylococcus aureus; CAPB = community-acquired bacterial pneumonia; CLSI = Clinical and Laboratory Standards Institute; MβL = Metallo-β-lactamase; MβL-PA = Metallo-β-lactamase-producing Pseudomonas aeruginosa; EUCAST = European Committee for Antimicrobial Susceptibility Testing; MIC = Minimum inhibitory concentration; MBC = Minimum bactericidal concentration; M sinh = MIC at subinhibitory point; MBC sinh = MBC at subinhibitory point; βL = β-lactamase; PA: CLSI = Penicillin/Amoxicillin; EUCAST = European Committee for Antimicrobial Susceptibility Testing; H. influenzae = Haemophilus influenzae; H. parainfluenzae = Hemophilus parainfluenzae; L. pneumophila = Legionella pneumophila; S. aureus = Staphylococcus aureus; S. pneumoniae = Streptococcus pneumoniae; E. coli = Escherichia coli; A. baumannii = Acinetobacter baumannii; K. pneumoniae = Klebsiella pneumoniae; M. catarrhalis = Moraxella catarrhalis; S. mutans = Streptococcus mutans; P. aeruginosa = Pseudomonas aeruginosa; AFB = Acid-Fast Bacilli; M. tuberculosis = Myco- cobacterium tuberculosis; M. bovis = Mycobacterium bovis; S. aureus = Staphylococcus aureus; S. epidermidis = Staphylococcus epidermidis; S. saprophyticus = Staphylococcus saprophyticus; M. abscessus = Mycobacterium abscessus; M. avium = Mycobacterium avium; M. kansasii = Mycobacterium kansasii; M. leprae = Mycobacterium leprae; M. gordonae = Mycobacterium gordonae; M. avium complex; L. pneumophila = Legionella pneumophila.