Bactericidal Action and Synergy Studies of BAL9141, A Novel Pyrrolidinone-3-ylidenemethyl Cephem, Tested Against Enterococci and Methicillin-Resistant Staphylococci (MRSA)

Background: BAL9141 has been reported to have inactivity against MSSA, many enterococci, and staphylococci with high-level penicillin resistance (HLP). In contrast, susceptibility to BAL9141 was retained in the presence of 8 µg/ml oxacillin or gentamicin. Clinical trials for BAL9141 appear against oxacillin-resistant vancomycin resistant enterococci tested using modest concentrations (8 µg/ml) were also tested in the same manner. Synergy was defined as ≥2 log decrease in the initial inoculum (approximately 5 x 10^8 CFU/ml) using BAL9141.

**MATERIALS AND METHODS**

The isolates were recent clinical isolates from bacteremic patients (SENTRY Antimicrobial Surveillance Program, 2002), standard quality control strains of well-characterized species, and the reference strains were from American Type Culture Collection, USA. The work was carried out in the microbiology laboratory at the Universidad de la República, Uruguay.

**RESULTS**

• BAL9141 showed a significant increase in the number of Enterococcus faecalis and E. faecium strains exhibiting an "Eagle-like effect" when tested alone with subinhibitory concentrations of gentamicin.

• All isolates were susceptible to vancomycin and teicoplanin.

• Clinical isolates were from bacteremic patients in the USA, Canada, Europe, and Latin America.

• Among isolates tested alone, significant differences were observed in the rate of killing based on MIC of the antimicrobial agent.

**CONCLUSIONS**

• BAL9141 showed significant activity against enterococci, methicillin-resistant Staphylococcus aureus (MSSA), and S. pneumoniae.

• Gentamicin showed synergy with BAL9141, although no differences were observed in some cases.

• The results warrant further clinical evaluation of this compound alone and in combination.

**SELECTED REFERENCES**

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