Comparative Antimicrobial Spectrum and Activity of BMS284756 (T-3811; A Desfluoroquinolone) Against Three Groups of Non-fermenting Gram-negative Bacilli, Including In Vitro Test Comparisons And Development

W. Howard, R.N. Jones, and D.J. Biedenbach.
University of Iowa, Iowa City, Iowa, USA; and The JONES Group, North Liberty, Iowa, USA.

ABSTRACT

Purpose: To compare the in vitro activity of BMS284756 (formerly T-3811), a desfluoroquinolone, with four other fluoroquinolones when tested against 129 Pseudomonas aeruginosa, 97 Stenotrophomonas maltophilia/Burkholderia spp. and Acinetobacter spp. Also in vitro test methods were compared for accuracy and reproducibility.

Methods: The BMS284756 MICs were determined using the broth microdilution method of the NCCLS and Etest (AB BIODISK, Solna, Sweden). These methods were compared for test accuracy and 5-µg disk diameters were compared for interpretative accuracy using the proposed susceptible breakpoint of ≤ 0.5 µg/ml (Fung-Tam et al. JAC 43:351-3556, 2000). All organisms tested were from the 1999-2000 SENTRY Antimicrobial Surveillance Program collection derived from medical centers in Europe and the Americas.

Results: Comparative fluoroquinolone potency against P. aeruginosa in the studied collection was as follows: desfluroquinolone (CIP; MIC 0.025 µg/ml) > gatifloxacin (GATI; MIC 0.03 µg/ml) > gemifloxacin (GEMI; MIC 0.03 µg/ml) = levofloxacin (LEV0; MIC 0.05 µg/ml) = trovafloxacin (TROV; MIC 0.05 µg/ml) = ciprofloxacin (CIP; MIC 0.05 µg/ml) = ofloxacin (OFLO; MIC 0.06 µg/ml). The BMS284756 MIC50, MIC90, and minimum inhibitory concentration (MIC) values for the Stenotrophomonas/Burkholderia spp. was 2 µg/ml. This potency was resistant to the susceptibility breakpoints for the other fluoroquinolones reported previously (Biedenbach et al. Eur J Clin Microbiol Infect Dis 19:428-431, 1999). The MICs results for the Acinetobacter spp. are as follows: CIP (≥0.5 µg/ml), GATI (4 µg/ml), GEMI (4 µg/ml), and BMS284756 (≥4 µg/ml). The Etest results compared favorably to the reference dilution test results for P. aeruginosa (100% ac. log2 dilutions) and for Acinetobacter spp. (100% ac. log2 dilutions), but the essential agreement rate was 100% (log2 dilutions). The disk diffusion test results compared well for the (a) ac. (0.04) without serious false-susceptible errors. The Stenotrophomonas/Burkholderia gr. strains also showed a maximum potential for major errors of only 0-3%. The disk diffusion test results demonstrated a wide spectrum of activity of BMS284756 against the three most commonly isolated species of non-fermenters from hospitalized patient infections. The results obtained from disk diffusion and Etest/AB BIODISK, Solna, Sweden) methods were also compared to those produced by the reference broth microdilution method described by the National Committee for Clinical Laboratory Standards (NCCLS).

RESULTS

Table 1. Activity of BMS284756 and four comparison quinolones tested against 279 strains of P. aeruginosa, Stenotrophomonas/Burkholderia gr. and Acinetobacter spp. Antimicrobial Spectrum and Activity of BMS284756 (T-3811; A Desfluoroquinolone) Against Three Groups of Non-Fermenting Gram-Negative Bacilli, Including In Vitro Test Comparisons and Development

Figures

Figure 1. Scatteredgrams comparing the BMS284756 MIC with the zone of inhibition around a 5-µg disk for the following: (a) P. aeruginosa, (129 strains); (b) Acinetobacter spp., 10 strains; and (c) Stenotrophomonas/Burkholderia spp., 60 strains. The zone diameter breakpoint criteria correlating to the proposed ≤ 0.5 µg/ml MIC including susceptibility.

RESULTS (continued)

Table 2. In vitro susceptibility of 4,106 positive blood stream infection isolates from North America, Latin America, and Europe to BMS284756, gatifloxacin, ciprofloxacin, and levofloxacin (Smedger, 2000).

CONCLUSIONS

• The Etest appears to be an excellent and practical alternative to the use of the reference broth microdilution method for BMS284756, a finding supported by similar success with this method for other quinolones. The disk diffusion method also provided results that appear acceptable for the proposed breakpoint for BMS284756 susceptibility (≤ 4 µg/ml) or a lower alternative ≤ 2 µg/ml.

SELECTED REFERENCES