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ABSTRACT

Objectives: To update the in vitro profile of dalbavancin (DALB), an investigational lipoglycopeptide, for its staphylococcal potency and spectrum of activity via the testing of a collection of clinical isolates from 2006-2009. A total of 62,590 staphylococcal isolates were evaluated (14,482 from the United States, 17,604 from the Asia-Pacific region, 11,692 from Europe, 16,011 from Latin America, and 28,186 from North America) from the Asia-Pacific region (11,692 strains), Europe (16,011), Latin America (6,711) and North America (28,186).

Methods: All organisms were susceptible (S) isolated by CLSI (2007-08) reference MIC methods in a central laboratory design. Staphylococcus spp. from 21 countries (201 medical centers in 21 nations) were sampled as follows: S. aureus (SA) (50,271 strains; 44.5% MRSA), and coagulase-negative staphylococci (CoNS; 12,373, 76.4% methicillin-resistant [MR], 23.6% susceptible [S]). DALB MIC results were determined in validated panels equivalent to reference polystyrene-80 (0.022) containing broth media. All QC results were within published ranges (CLSI M100-S21, 2011). Most isolates came from blood (63.0%), lower respiratory or acute bacterial skin and skin structure infection (ABSSSI) sources.

RESULTS: DALB was highly active against SA (MIC<sub>90</sub> ≤ 0.06 mg/L) with a 1 mg/L MBC. All strains were inhibited at ≤ 0.25 mg/L. DALB was more active than vancomycin, linezolid, daptomycin, and teicoplanin against most staphylococcal strains. DALB activity (Table) and DALB potency remained consistent across all geographical regions. Conclusions

Dalbavancin (BI-397, MDL E339, AA1, VER001) is a monoantimicrobial glycopeptide containing a novel morpholino cyclic ether, derived from the natural glycopeptide A40926 produced by 3,3- dimethylamino-3-hexylmethylmorpholino substitution on the peptidoglycan precursor, which is similar to other lipoglycopeptides in its mechanism of activity, binding to the terminal alanyl-DAla of intact peptidoglycan chains and thus interfering with bacterial cell wall biosynthesis and resulting in cell death. Previous studies have demonstrated the potent activity of dalbavancin against aeroebic and anaerobic Gram-positive organisms, including such clinically relevant strains as methicillin-resistant (MR) Staphylococcus spp., vancomycin-resistant enterococci (VRE), daptomycin resistant Staphylococcus pneumoniae and vancomycin-resistant enterococci (VRE). The MICs of dalbavancin (DALB) were found to be equal or lower than those of vancomycin, linezolid, daptomycin, and teicoplanin against S. aureus and staphylococci of other species. DALB was highly active against SA (MIC<sub>50</sub>/90, 0.06/0.12 mg/L) and CoNS (MIC<sub>50</sub>/90, 0.25/0.5 mg/L). DALB was highly active against SA (MIC<sub>50</sub>/90, 0.06/0.12 mg/L) and CoNS (MIC<sub>50</sub>/90, 0.25/0.5 mg/L). DALB activity (Table) and DALB potency remained consistent across all geographical regions.

Susceptibility testing: The MIC results were generated by the reference-quality Clinical and Laboratory Standards Institute (CLSI) National Committee for Clinical Laboratory Standards (NCCLS). The assay was performed in 96-well microtiter plates using broth dilution antimicrobial susceptibility tests for bacteria that grow aerobically; plates containing Mueller-Hinton, with sub-inhibitory concentrations of dalbavancin and linezolid. Susceptibility testing was performed using Clinical and Laboratory Standards Institute (CLSI) broth microdilution methods and interpreted according to CLSI breakpoints. The results are reported as percent of isolates inhibited at each test concentration. The MIC<sub>50</sub> and MIC<sub>90</sub> were determined for each strain against dalbavancin. The MIC<sub>50</sub> and MIC<sub>90</sub> for dalbavancin were ≤ 0.25 mg/L and ≤ 0.12 mg/L, respectively. DALB activity (Table) and DALB potency remained consistent across all geographical regions.


Figure 1. MIC distribution for dalbavancin tested against staphylococci (62,590 strains) 2007-2009 worldwide.

REFERENCES


Dalbavancin activity and spectrum evaluated against a contemporary (2007-2009) worldwide collection of staphylococci (62,590 strains)

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