Antimicrobial Activity of Telavancin Against Enterococcus faecalis, E. faecium and E. avium: Results From a European Surveillance Program (2007)

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ABSTRACT

Objectives. To evaluate the potency of telavancin against enterococcal isolates (Enterococcus faecalis [EF], E. faecium [EFM] and E. avium [EAv]) collected as part of a European surveillance protocol for 2007. Telavancin is an investigational, intravenous, semi-synthetic, beta-lactamglycopeptide that is broadly active against both enterococci and anerobic Gram-positive bacteria. The agent has been evaluated in two Phase 3 clinical trials and is currently awaiting regulatory approval.

Methods. Non-duplicate clinical isolates (191 total), see Table of EF (875), EFM (308) and EAv (62) were submitted from 26 medical centers in Europe participating in telavancin surveillance. Identities were confirmed by the central control and all isolates were susceptibility tested using Clinical and Laboratory Standards Institute broth microdilution methods.

Results. The antimicrobial activity of EF against Year 2007 enterococcal isolates is shown in the Table. Among the comparator agents, telavancin was the most potent agent tested against Enterococcus spp. (EF and EFM), MIC values, (0.25 and 0.06 mg/L, respectively) compared to vancomycin (1 and 1 mg/L), daptomycin (1 and 2 mg/L) and levofloxacin (1, 1 and 0.5 mg/L), respectively. Overall, 9.7% of tested enterococci were vancomycin-resistant, including 1.0% of EF and 2.5% of EFM (MIC values >1 µg/mL compared to 20.6% of tested vancomycin-resistant, including 1.0% of EF and 25.8% of EFM; telavancin remained 16-fold more potent than vancomycin against these three resistant EFM strains).

Telavancin is bactericidal by means of inhibition of bacterial cell wall synthesis and disruption of bacterial membranes function. Efficacy and safety of telavancin have been demonstrated in Phase 2 and 3 clinical trials and skin-structure clinical trials. Telavancin is the only investigational agent with activity against acidic enterococci, vancomycin-resistant enterococci (VRE) strains.

This poster summarizes the 2007 results of an international surveillance testing program comparing the activity of telavancin and currently marketed glycopeptides with other antimicrobial agents against enterococcal clinical isolates submitted from medical centres located in Europe in 2007.

MATERIALS AND METHODS

Bacterial strain collection. 2,395 non-duplicate, consecutive enterococcal clinical isolates were submitted from 26 medical centres located in Europe as part of an international surveillance programme for 2007.

Isolates originated predominantly from patients with documented bloodstream, respiratory tract and skin and soft tissue infections. The distribution of loading species included E. faecalis (791 isolates), E. faecium (1308) and E. avium (12). Isolates were confirmed by the central control (JMI Laboratories, North Liberty, Iowa, USA).

INTRODUCTION

The dramatic spread of methicillin-resistant Staphylococcus aureus (MRSA) infections into the hospital environment, including strains characteristically found in the community (community-acquired), has significantly changed antimicrobial prescribing practices in recent years.

In increased use of vancomycin for treating staphylococcal infections has driven rates of vancomycin-resistant enterococci (VRE) to high levels in some regions, and has produced an increase in S. aureus that are non-susceptible to vancomycin (most commonly heterogeneous vancomycin-intermediate, S. aureus (VI-VA), but also VISA and some vancomycin-resistant (VRE) strains).

The timely development and introduction of new agents with potency and pharmacokinetic/pharmacodynamic properties that can prevent further resistance emergence among enterococci and staphylococci are sorely needed.

Telavancin is an investigational, parenteral, semi-synthetic, beta-lactamglycopeptide that is broadly active against enterococci and anerobic Gram-positive bacteria, including S. aureus and coagulase-negative staphylococci (methicillin-susceptible and -resistant strains), streptococci (including viridans group streptococci (VGS) strains).1,2

Telavancin was bactericidal by means of inhibition of bacterial cell wall synthesis and disruption of bacterial membranes function. Efficacy and safety of telavancin have been demonstrated in Phase 2 and 3 clinical trials and skin-structure clinical trials.1,2,4 Phase 3 Trials for nosocomial pneumonia have been completed.

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Telavancin was submitted to the US FDA by the manufacturer (Teva Pharmaceuticals, Tel Aviv, Israel) in assessing the long-term efficacy of this promising agent.

RESULTS

Among tested agents, telavancin was one of the most active against E. faecalis, E. faecium and E. avium, with 0.25 and 0.06 mg/L, respectively. Table 1 and 2 compared with vancomycin (1 and 0.5 mg/L), daptomycin (1 and 2 mg/L) and levofloxacin (1, 1 and 0.5 mg/L), respectively. Table 2.

One drawback of telavancin is that it is not indicated for use against E. faecalis and E. faecium and is therefore not indicated for use against VRE strains.

Evaluation of resistance emergence among enterococci and staphylococci are further resistance emergence in problematic enterococci and other Gram-positive bacteria, including S. aureus and coagulase-negative staphylococci (methicillin-susceptible and -resistant strains), streptococci (including viridans group streptococci (VGS) strains).1,2

Telavancin inhibited 94.0% of strains at ≤0.06 mg/L of telavancin.

CONCLUSIONS

Based on MIC50, telavancin was the most active agent tested against contemporary (2007) European Enterococcus spp. isolates. Telavancin inhibited 94.0% of strains at ≤0.06 mg/L, whereas only 88.9% were inhibited by all 4 agents of vancomycin (current CLSI breakpoints).

Overall, 9.7% of tested enterococci were vancomycin-resistant, including 1.0% of E. faecalis, 2.5% of E. faecium and 8.3% of E. avium. Telavancin remained 16-fold more active (MIC90) than vancomycin against the commonest resistant E. faecium isolates in Europe.

Continued monitoring for resistance emergence in problematic pathogens, especially enterococci and staphylococci, will be critical in assessing the long-term efficacy of this promising agent.

REFERENCES