


In-vitro activity of quinupristin/dalfopristin (Synercid) against isolates of Streptococcus pneumoniae, Staphylococcus aureus and Enterococcus spp.


A. P. Johnson*, M. Warner and D. C. E. Speller

Antibiotic Reference Unit, Laboratory of Hospital Infection, Central Public Health Laboratory, Colin-dale, London NW9 5HT, UK

*Corresponding author. Tel: +44-181-200-4400; Fax: +44-181-200-7449; E-mail: ajohnson@phls.co.uk

Sir,

The emergence and spread of antibiotic-resistant Gram-positive bacteria, including penicillin- and erythromycin-resistant pneumococci, methicillin-resistant Staphylococcus aureus (MRSA) and glycopeptide-resistant enterococci, are posing increasingly difficult therapeutic problems, particularly in hospitals. For this reason, there is a continuing need for the development of new antimicrobial agents with activities against bacteria that are resistant to currently available drugs. We report here the results of a study of the in-vitro activity of quinupristin/dalfopristin against isolates of Streptococcus pneumoniae, S. aureus and Enterococcus spp. submitted to the Central Public Health Laboratory (CPHL) from hospitals in the UK during 1995 and 1996. As a common reason for referral of isolates to the CPHL is confirmation of antibiotic resistance, a significant proportion of the isolates tested were resistant to one or more antibiotics (Table).

Quinupristin/dalfopristin was supplied by Rhône–Poulenc Rorer (West Malling, UK) and the MICs were determined by an agar dilution method described by the National Committee for Clinical Laboratory Standards.

Quinupristin/dalfopristin exhibited good activity against S. pneumoniae, with MICs falling in the range 0.25–4 mg/L; the MIC_{50} and MIC_{90} were 0.5 mg/L and 1 mg/L, respectively. The distribution of the MICs of quinupristin/dalfopristin for pneumococci that were resistant to either penicillin or erythromycin overlapped markedly with those for isolates that were susceptible to these agents. For isolates of S. aureus, MICs were in the range 0.25–1 mg/L (MIC_{50} and MIC_{90} 1 mg/L). There was no difference between staphylococci that were resistant to methicillin and those that were susceptible in terms of susceptibility to quinupristin/dalfopristin.

Quinupristin/dalfopristin also exhibited good activity against several species of enterococci. The MICs for 50 of the 51 isolates of Enterococcus faecium were either 0.5 or 1 mg/L, the MIC for the remaining isolate being 4 mg/L. The MICs for the four strains of Enterococcus avium and six strains of Enterococcus gallinarum ranged from 1 to 2 mg/L and from 2 to 4 mg/L, respectively, and the MICs for all five isolates of Enterococcus raffinosus were 2 mg/L. Quinupristin/dalfopristin was much less active against the Enterococcus faecalis strains than other enterococci. MICs falling within the range 8–32 mg/L. The MICs of quinupristin/dalfopristin for the five strains of Enterococcus casseliflavus were between 2 and 8 mg/L.

Quinupristin/dalfopristin exhibited comparable activity against isolates of enterococci, regardless of their susceptibilities to other antimicrobial agents such as glycopeptides and gentamicin (high-level).

Although a breakpoint that defines resistance to quinupristin/dalfopristin has not yet been formally agreed, some investigators have used a provisional value of 4 mg/L, based on pharmacokinetic parameters. According to this breakpoint, all of the strains of S. pneumoniae, S. aureus, E. faecium, E. avium, E. gallinarum and E. raffinosus tested in the present study would be considered susceptible to quinupristin/dalfopristin, whereas the 16 strains of E. faecalis would be classified as resistant. The five E. casseliflavus strains clustered around the provisional breakpoint, with two being susceptible and three resistant. Others have reported similar activities for quinupristin/dalfopristin against these species.

The activities of quinupristin/dalfopristin against a wide range of Gram-positive pathogens, including pneumococci, staphylococci and some species of enterococci, mean that this drug might be a useful addition to the current antibiotic armamentarium. The observations made both in the present study and by others that quinupristin/dalfopristin is active in vitro against bacteria that are resistant to other antibiotics, such as penicillin- and/or erythromycin-resistant pneumococci, MRSA and glycopeptide-resistant enterococci, suggest that this agent might be particularly useful in clinical settings where the therapeutic options are limited by problems of resistance.
Correspondence

Table. Antimicrobial resistance patterns of the study strains

<table>
<thead>
<tr>
<th>Bacterium (no. of strains)</th>
<th>Percentage of isolates of intermediate susceptibility or fully resistant to indicated agent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amp</td>
</tr>
<tr>
<td>S. pneumoniae (86)</td>
<td>NT</td>
</tr>
<tr>
<td>S. aureus (78)</td>
<td>NT</td>
</tr>
<tr>
<td>E. faecium (51)</td>
<td>100</td>
</tr>
<tr>
<td>E. faecalis (16)</td>
<td>0</td>
</tr>
<tr>
<td>E. avium (4)</td>
<td>0</td>
</tr>
<tr>
<td>E. casseliflavus (5)</td>
<td>0</td>
</tr>
<tr>
<td>E. gallinarum (6)</td>
<td>0</td>
</tr>
<tr>
<td>E. raffinosus (5)</td>
<td>5</td>
</tr>
</tbody>
</table>

*Refers to high-level gentamicin resistance.
 Abbreviations: Amp, ampicillin; Pen, penicillin; Met, meticillin; Gen, gentamicin; Van, vancomycin; Tei, teicoplanin; Ery, erythromycin; Cip, ciprofloxacin; Chl, chloramphenicol; Rif, rifampicin; Dox, doxycycline; QD, quinupristin/dalfopristin; NT, not tested.

Acknowledgement

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References


Antimicrobial activity of LB20304, a fluoronaphthyridone, tested against anaerobic bacteria

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Francesc Marco†, Mary S. Barrett and Ronald N. Jones*

†Present address: Microbiology Laboratory, Hospital Clinic, University of Barcelona, Villarroel 170, 08036-Barcelona, Spain.

*Corresponding author. Tel: +1-319-356-2990; Fax: +1-319-356-4916.

Sir,

Most currently available fluoroquinolones exhibit limited or negligible activity against some Gram-positive aerobic and many anaerobic bacterial pathogens. In the last few years, however, newer fluoroquinolone compounds have been synthesized that have improved activity against these microorganisms while retaining broad-spectrum activity against Gram-negative bacilli.1-3

LB20304 is a novel fluoronaphthyridone that contains a pyrrolidine substitution.4 An animal model study has documented reduced central nervous system toxicity for LB20304 compared with ciprofloxacin or ofloxacin and good bioavailability after oral administration.5 LB20304 activity against most species of Enterobacteriaceae and *Pseudomonas aeruginosa* is two- to four-fold less than ciprofloxacin.6-8 Against Gram-positive organisms...