In Vitro Activity of ABT-773, a New Ketolide, against Recent Clinical Isolates of Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis

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The in vitro activity of ABT-773 was evaluated against Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis isolates. ABT-773 was the most active antimicrobial tested against S. pneumoniae. ABT-773 and azithromycin were equivalent in activity against H. influenzae and M. catarrhalis and more active than either clarithromycin or erythromycin.

ABT-773 (A-195773) is a new ketolide having a potent antibacterial spectrum including activity against penicillin- and macrolide-resistant gram-positive bacteria. Its chemical name is 11-amino-11-deoxy-3-oxo-5-[[1'-49247, 49766, and 10211; and

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5). Prior to testing, organisms having been stored at

isolates. Details of this study have been reported previously (1, 2, 70°C

national surveillance study conducted from 1 November 1997

TABLE 1. ABT-773 was the most active of the seven anti-

crobials tested: 78.9% of S. pneumoniae isolates were inhibited

by ABT-773 at a concentration of ≤0.008 μg/ml. The MIC at

which 90% of the isolates were inhibited (MIC90) was 0.03

μg/ml. The highest ABT-773 MIC was 0.5 μg/ml (n = 3).

When isolates were sorted according to penicillin susceptibility
category, the ABT-773 MIC90s were as follows: penicillin sus-

ceptible (penicillin MIC, ≤0.06 μg/ml), ≤0.008; penicillin

intermediate (penicillin MIC = 0.12 to 1 μg/ml), 0.03; and

penicillin resistant (penicillin MIC, ≥2 μg/ml), 0.12 μg/ml.

Comparison compounds included the macrolides erythromycin,

clarithromycin, and azithromycin and a lincosamide, clindamycin.

The MIC50s and MIC90s and ranges of MICs obtained

with these agents were 0.06, 8, and ≤0.03 to >64; ≤0.03, 4,

and ≤0.03 to >64; 0.12, 16, and ≤0.03 to >64; and 0.06,

0.06, and ≤0.008 to >8 μg/ml, respectively.

Table 2 depicts the relationship between ketolide and eryth-

romycin MICs. S. pneumoniae has two principal mechanisms of

macrolide resistance, efflux and constitutively expressed mac-

rolide-lincosamide-streptogramin B resistance as a result

of ribosomal alterations (2, 6). Efflux, the result of expression

of the mefE gene, usually results in erythromycin MICs of 1 to 32

μg/ml and clindamycin MICs of ≤0.25 μg/ml (1). Altered ri-

bosomal targets as a consequence of erm/EM gene-mediated

Strains for which erythromycin MIC is ≤0.5 μg/ml are erythromycin susceptible or intermediate; strains for which erythromycin MIC is 1 to 32 μg/ml and clindamycin MIC is ≤0.25 have the efflux phenotype; strains for which erythromycin MIC is ≥64 μg/ml and clindamycin MIC is ≥8 μg/ml have the ermAM genotype.

The results of the current study indicate that ABT-773, a new ketolide antimicrobial agent, has potent in vitro activity against recent clinical isolates of S. pneumoniae. Although the drug is less active against H. influenzae and M. catarrhalis, the overall activity of ABT-773 against these three pathogens would be sufficient to warrant performance of clinical trials with patients with respiratory tract infections due to these organisms, assuming acceptable pharmacokinetic and toxicity profiles.
This investigation was funded by a grant from Abbott Laboratories.

REFERENCES


### TABLE 3. Comparison of the in vitro activities of ABT-773 and the macrolides against 1,529 isolates of *H. influenzae* and 726 isolates of *M. catarrhalis*.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antimicrobial agent</th>
<th>Value for strain type:</th>
<th>Beta-lactamase positive</th>
<th>Beta-lactamase negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MIC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>MIC&lt;sub&gt;90&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>ABT-773</td>
<td>2</td>
<td>4</td>
<td>0.12–8</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
<td>2</td>
<td>4</td>
<td>0.25–64</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>8</td>
<td>16</td>
<td>0.5–128</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>8</td>
<td>16</td>
<td>0.25–64</td>
</tr>
<tr>
<td><em>M. catarrhalis</em></td>
<td>ABT-773</td>
<td>0.06</td>
<td>0.06</td>
<td>≤0.004–0.12</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
<td>0.06</td>
<td>0.12</td>
<td>0.03–0.25</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>0.12</td>
<td>0.12</td>
<td>≤0.015–0.5</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>0.25</td>
<td>0.25</td>
<td>0.06–1</td>
</tr>
</tbody>
</table>

* For beta-lactamase-positive strains, n = 476 for *H. influenzae* and 687 for *M. catarrhalis*; for beta-lactamase-negative strains, n = 1,053 for *H. influenzae* and 39 for *M. catarrhalis*. MICs are expressed as micrograms per milliliter. % I, percent intermediate; % R, percent resistant.