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In Vitro Activities of BMS-284756 against *Chlamydia trachomatis* and Recent Clinical Isolates of *Chlamydia pneumoniae*

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The in vitro activities of BMS-284756 (a novel des-fluoroquinolone), levofloxacin, moxifloxacin, and clarithromycin were tested against 5 strains of *Chlamydia trachomatis* and 20 isolates of *Chlamydia pneumoniae*. The MIC at which 90% of the isolates were inhibited and the minimal bactericidal concentration at which 90% of the isolates were killed by BMS-284756 for all isolates of *C. pneumoniae* and *C. trachomatis* was 0.015 μg/ml (range, 0.015 to 0.03 μg/ml). BMS-284756 was the most active quinolone tested.

Chlamydia pneumoniae is a frequent cause of community-acquired respiratory tract infection, including pneumonia and bronchitis, in adults and children. Quinolones have attracted interest as therapy for community-acquired respiratory tract infections because they are active against a wide range of pathogens responsible for these diseases, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Mycoplasma pneumoniae* (1, 3, 9, 11). We previously reported that quinolones, including ofloxacin, levofloxacin, grepafloxacin, gatifloxacin, gemifloxacin, sparfloxacin, trovafloxacin, and moxifloxacin, have good activity against *Chlamydia trachomatis* and *C. pneumoniae* in vitro (4–8). BMS-284756 is a novel des-fluoro(6) quinolone, which differs from recently approved quinolones in that it lacks fluorine at the C-6 position. BMS-284756 has antibacterial activity similar to that of other fluorinated quinolones against most bacteria (3). We compared the in vitro activity of BMS-284756, levofloxacin, moxifloxacin, and clarithromycin against 5 strains of *C. trachomatis* and 20 recent clinical isolates of *C. pneumoniae.*

Strains of *C. trachomatis* included E-BOUR (ATCC VR-384B), F-IC-CAL3 (ATCC VR-346), C-HAR32 (ATCC VR-572), J-UW-36 (ATCC VR-886), and $L_2$434 (ATCC VR-902B). Isolates of *C. pneumoniae* tested included one reference isolate; TW183 (ATCC VR-2282; Washington Research Foundation, Seattle, Wash.); CM-1, a clinical isolate from the Centers for Disease Control and Prevention (ATCC VR-1360); and 18 recent clinical isolates from adults and children enrolled in multicenter community-acquired pneumonia treatment studies conducted in the United States: T2023 (ATCC VR-1356), 124, 453, 490, 493, 600, 08002, 08016, 21001, 21002, 2212, 24013, 25001, MC16005, MC01016, MT57001, PDS07015, and RR57002. BMS-284756 (Bristol-Myers Squibb, Wallingford, Conn.), levofloxacin (Ortho Pharmaceuticals, Raritan, N.J.), moxifloxacin (Bayer Pharmaceuticals, West Haven, Conn.), and clarithromycin (Abbott Laboratories, Abbott Park, Ill.) were supplied as powders and were solubilized according to the manufacturers' instructions. Susceptibility testing of *C. trachomatis* and *C. pneumoniae* was performed in cell culture with HEp-2 cells grown in 96-well microtiter plates as previously described (5). Each experiment was set up in duplicate plates. Each well was inoculated with 0.1 ml of the test organism diluted to yield 10^3 to 10^4 inclusion-forming units (IFU) per ml for a multiplicity of infection of 1:1, was centrifuged at 1,700 × *g* for 1 h, and was incubated at 35°C for 1 h. Wells were then aspirated and overlaid with 0.2 ml of medium (Iscove's modification of Dulbecco's modified Eagle's medium) containing 1 μg of cycloheximide per ml and serial twofold dilutions of the test drug. After incubation at 35°C for 72 h, the cultures in one plate were fixed and stained for inclusions with fluorescein-conjugated antibody to the lipopolysaccharide genus antigen (Pathfinder; Bio-Rad Labs, Hercules, Calif.). The MIC was the lowest antibiotic concentration at which no inclusions were seen. The minimal bactericidal concentration (MBC) was determined by aspirating the antibiotic-containing medium of the second plate, washing wells twice with phosphate-buffered saline, and adding antibiotic-free medium. Cultures were frozen at −70°C, thawed, passed onto fresh new cells, incubated for 72 h, and then fixed and stained as above. The MBC was the lowest antibiotic concentration that resulted in no inclusions after passage. Three replicates were conducted for each assay.

The MICs and MBCs for *C. trachomatis* are shown in Table 1. The MICs and MBCs for *C. trachomatis* were the following: BMS-284756, 0.015 μg/ml; levofloxacin, 0.5 μg/ml; moxifloxacin, 0.5 μg/ml; and clarithromycin, 0.03 μg/ml. The MIC and MBCs for *C. pneumoniae* are shown in Table 2. The MICs at which 90% of the isolates tested are inhibited and the MBCs at which 90% of the strains tested are killed for *C. pneumoniae* were the following: BMS-284756, 0.015 μg/ml; levofloxacin, 0.5 and 1.0 μg/ml; moxifloxacin, 0.5 and 1.0 μg/ml; and clarithromycin, 0.03 and 0.06 μg/ml. The MICs obtained for BMS-284756 against *C. trachomatis* and *C. pneumoniae* in the present study were very consistent, especially in view of the wide geographic distribution of the isolates tested.

Fung-Tomc et al. (3) reported that BMS-284756 was the most active quinolone tested against a wide range of bacteria. They tested 10 isolates of *C. trachomatis*, and the MICs were ≤0.004 to 0.016 μg/ml. Fung-Tomc et al. (3) also tested 4 isolates of *C. pneumoniae*, and the MICs were ≤0.004 to 0.008 μg/ml. The isolates tested were not specified, nor were the

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TABLE 1. Activities of BMS-28476 and other antibiotics against 5 strains of *C. trachomatis*

Strain	Drug MIC and MBC[a]							
	BMS-28476		Levofloxacin		Moxifloxacin		Clarithromycin	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
E-BOUR	0.015	0.015	0.5	0.5	0.5	0.5	0.03	0.03
F-IC-CAL3	0.015	0.015	0.5	0.5	0.5	0.5	0.03	0.03
C-HAR32	0.015	0.015	0.5	0.5	0.5	0.5	0.03	0.03
J-UW-36	0.015	0.015	0.5	0.5	1	1	0.03	0.03
$L_2$434	0.015	0.015	0.5	0.5	0.5	0.5	0.03	0.03

[a] 50% MIC and MBC for isolates in micrograms/milliliter.

methods described, but their results were almost identical to ours.

The 1998 Centers for Disease Control Guidelines for the Treatment of Sexually Transmitted Diseases lists ofloxacin (300 mg orally twice a day for 7 days) as an alternative regimen for the treatment of uncomplicated genital *C. trachomatis* infection in adolescents and adults (2). Ofloxacin is similar in efficacy to doxycycline and azithromycin but is more expensive and offers no advantage with regard to dosing and the length of treatment (2). Based on its in vitro activity and pharmacokinetics (3), BMS-284756 should have equivalent if not better efficacy for treatment of *C. trachomatis* infections.

Data are limited on the efficacy of quinolones for treatment of *C. pneumoniae* infections. The majority of studies, especially for treatment of community-acquired pneumonia, have based the diagnosis of *C. pneumoniae* on serology; thus, microbiologic efficacy could not be assessed. However, results from two multicenter treatment studies of community-acquired pneumonia found that levofloxacin and moxifloxacin had 70 to 80% efficacy in the eradication of *C. pneumoniae* from the nasopharynx (6, 8). The MICs and MBCs for the *C. pneumoniae* isolates obtained from these patients after treatment were the same as those obtained before treatment, suggesting that persistence was not due to the development of resistance. These findings are similar to reported experiences with erythromycin, clarithromycin, and azithromycin (7, 10). BMS-284756 is the most active quinolone tested thus far and is more active than clarithromycin and azithromycin. Prospective studies of BMS-284756 for the treatment of genital chlamydia infections and community-acquired pneumonia utilizing culture of *C. trachomatis* and *C. pneumoniae* will determine the role of BMS-284756 in the treatment of these infections.

TABLE 2. Activities of BMS-28476 and other antibiotics against 20 isolates of *C. pneumoniae*

Drug	MIC (μg/ml)[a]			MBC (μg/ml)[a]	
	Range	50%	90%	Range	90%
BMS-28476	0.015–0.03	0.015	0.015	0.015–0.03	0.015
Levofloxacin	0.5–1.0	0.5	1.0	0.5–1.0	1.0
Moxifloxacin	0.125–1.0	0.5	1.0	0.125–1.0	1.0
Clarithromycin	0.015–0.06	0.03	0.06	0.015–0.06	0.06

[a] 50% and 90%, MIC and MBC for 50% and 90% of isolates, respectively.

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