In Vitro Activities of Tigecycline against the *Bacteroides fragilis* Group

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The in vitro activities of tigecycline were tested against 831 isolates of the *Bacteroides fragilis* group representing all of the species within the group. On a weight-to-weight basis (8 μg/ml), tigecycline was more active than clindamycin, minocycline, trovafloxacin, and cefoxitin and less active than imipenem or piperacillin-tazobactam against all isolates of the *B. fragilis* group. Tigecycline geometric mean MICs were statistically higher against *B. distasonis* than other *Bacteroides* species (P value of 0.0001).

The use of tetracyclines against anaerobic or mixed infections has been limited by the increased resistance of anaerobic bacteria against this class of antibiotics. Tigecycline (GAR-936), a new glycylcycline derivative of minocycline, has shown excellent in vitro activities against a broad spectrum of aerobic bacteria containing tetracycline-resistant elements (2, 4, 7, 8, 13). Reports from the literature also show good antianaerobic activity, including against members of the *Bacteroides fragilis* group. Tigecycline, while only 39.2% were inhibited by minocycline. At the same concentration, tigecycline inhibited a comparable percentage (87.4%). Imipenem and piperacillin-tazobactam were the most active drugs in the evaluation. At their NCCLS-suggested breakpoints for resistance (16 μg/ml for imipenem and 128 and 4 μg/ml, respectively, for piperacillin and tazobactam in combination), there were no strains resistant to piperacillin-tazobactam and only one strain resistant to imipenem.

Analysis of the data by species showed that the MICs for *B. distasonis* were statistically significantly higher than those for
### TABLE 1. Activity of tigecycline and comparator agents against *B. fragilis* and related species

<table>
<thead>
<tr>
<th>Species (no. of strains)</th>
<th>Antibiotic</th>
<th>MIC range (µg/ml)</th>
<th>MIC (µg/ml)</th>
<th>% of isolates for which MIC (µg/ml) was ≥</th>
<th>% Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥1</td>
<td>≥2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>90</td>
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</tr>
</tbody>
</table>

#### B. distasonis (98)
- **Tigecycline**: 0.5–8, 4 | 8 | 93.9 | 81.6 | 56.1 | 11.2 | 0 | NA
- **Minocycline**: 0.25–32, 8 | 16 | 81.6 | 76.5 | 74.5 | 56.1 | 20.4 | NA
- **Clindamycin**: 0.5–128, 1 | 128 | 25.5 |
- **Trovafloxacin**: 0.06–16, 2 | 8 | 25.5 |
- **TZP**<sup>c</sup>: 0.5–64, 8 | 16 | 25.5 |
- **Imipenem**: 0.125–16, 1 | 2 | 1.0 |
- **Cefoxitin**: 2–256, 32 | 64 | 33.7 |

#### B. fragilis (289)
- **Tigecycline**: 0.25–32, 2 | 4 | 86.9 | 56.7 | 19.4 | 10.0 | 4.8 | NA
- **Minocycline**: 0.25–64, 8 | 32 | 81.7 | 79.6 | 77.5 | 67.1 | 45.7 | NA
- **Clindamycin**: 0.5–128, 0.5 | 128 | 16.3 |
- **Trovafloxacin**: 0.25–16, 0.5 | 8 | 20.1 |
- **TZP**: 0.5–64, 1 | 4 | 0 |
- **Imipenem**: 0.125–8, 0.25 | 1 | 0 |
- **Cefoxitin**: 2–128, 32 | 64 | 3.5 |

#### B. ovatus (90)
- **Tigecycline**: 0.25–16, 2 | 4 | 75.6 | 52.2 | 28.9 | 10.0 | 2.2 | NA
- **Minocycline**: 0.25–64, 8 | 16 | 81.1 | 80.0 | 76.7 | 56.7 | 23.3 | NA
- **Clindamycin**: 0.5–128, 2 | 128 | 31.1 |
- **Trovafloxacin**: 0.5–16, 2 | 8 | 14.4 |
- **TZP**: 0.5–32, 4 | 16 | 0 |
- **Imipenem**: 0.125–4, 0.25 | 1 | 0 |
- **Cefoxitin**: 4–128, 32 | 64 | 18.9 |

#### B. thetaiotaomicron (185)
- **Tigecycline**: 0.25–16, 2 | 4 | 87.0 | 58.4 | 25.4 | 10.8 | 2.2 | NA
- **Minocycline**: 0.25–32, 8 | 16 | 75.7 | 73.5 | 70.8 | 55.1 | 21.1 | NA
- **Clindamycin**: 0.5–128, 2 | 128 | 27.0 |
- **Trovafloxacin**: 0.5–32, 1 | 8 | 22.7 |
- **TZP**: 0.5–64, 8 | 16 | 0 |
- **Imipenem**: 0.125–4, 0.25 | 1 | 0 |
- **Cefoxitin**: 4–128, 32 | 64 | 15.7 |

#### B. uniformis (26)
- **Tigecycline**: 0.25–8, 1 | 2 | 65.4 | 34.6 | 3.8 | 3.8 | 0 | NA
- **Minocycline**: 0.25–32, 8 | 16 | 80.8 | 76.9 | 76.9 | 57.7 | 19.2 | NA
- **Clindamycin**: 0.5–128, 1 | 128 | 23.1 |
- **Trovafloxacin**: 0.5–8, 2 | 8 | 26.9 |
- **TZP**: 0.5–16, 2 | 16 | 0 |
- **Imipenem**: 0.125–1, 0.25 | 0.5 | 0 |
- **Cefoxitin**: 0.5–32, 2 | 16 | 0 |

#### B. vulgatus (86)
- **Tigecycline**: 0.5–8, 1 | 4 | 75.6 | 43.0 | 17.4 | 7.0 | 0 | NA
- **Minocycline**: 0.25–32, 8 | 16 | 74.4 | 73.3 | 72.1 | 64.0 | 25.6 | NA
- **Clindamycin**: 0.5–128, 0.5 | 128 | 27.9 |
- **Trovafloxacin**: 0.25–32, 4 | 16 | 44.2 |
- **TZP**: 0.5–32, 4 | 8 | 0 |
- **Imipenem**: 0.125–4, 0.25 | 0.5 | 0 |
- **Cefoxitin**: 4–128, 8 | 64 | 10.5 |

#### Other Bacteroides spp. (57)<sup>d</sup>
- **Tigecycline**: 0.5–64, 1 | 8 | 82.5 | 49.1 | 24.6 | 17.5 | 7.0 | NA
- **Minocycline**: 0.25–64, 8 | 32 | 80.7 | 78.9 | 77.2 | 57.9 | 28.1 | NA
- **Clindamycin**: 0.5–128, 1 | 128 | 19.3 |
- **Trovafloxacin**: 0.125–16, 1 | 8 | 14.0 |
- **TZP**: 0.5–32, 4 | 16 | 0 |
- **Imipenem**: 0.125–4, 0.25 | 1 | 0 |
- **Cefoxitin**: 4–256, 32 | 64 | 12.3 |

#### All *B. fragilis* group species combined (831)
- **Tigecycline**: 0.25–64, 2 | 8 | 84.4 | 56.9 | 25.8 | 10.3 | 2.9 | NA
- **Minocycline**: 0.25–64, 8 | 16 | 79.4 | 77.1 | 75.0 | 60.8 | 30.7 | NA
- **Clindamycin**: 0.5–128, 1 | 128 | 23.0 |
- **Trovafloxacin**: 0.06–32, 1 | 8 | 23.0 |
- **TZP**: 0.5–64, 4 | 16 | 0 |
- **Imipenem**: 0.125–16, 0.5 | 1 | 0.1 |
- **Cefoxitin**: 2–256, 16 | 64 | 12.6 |

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<sup>a</sup> NCCLS has not established breakpoints for resistance for tigecycline and minocycline.

<sup>b</sup> Resistance based on NCCLS-established breakpoints for fully resistant: cefoxitin, ≥64 µg/ml; clindamycin and trovafloxacin, ≥8 µg/ml; imipenem ≥16 µg/ml; piperacillin-tazobactam, ≥128 µg/ml.

<sup>c</sup> NA, not applicable.

<sup>d</sup> TZP, piperacillin-tazobactam.

<sup>e</sup> Includes 53 *B. caccae*, 1 *B. eggerthii*, 1 *B. mordaci* and 2 *B. stercoralis* strains.

<sup>f</sup> 50 and 90, MIC<sub>50</sub> and MIC<sub>90</sub> respectively.
the other Bacteroides species (P value of 0.0001 as calculated by a nonparametric Kruskal-Wallis test). The geometric mean MIC (MIC<sub>GM</sub>) of 2.69 µg/ml was approximately twice the MIC<sub>GM</sub> for the other species (data not shown in Table 1). The MIC range for this species, however, was not the highest. The highest MICs (32 and 64 µg/ml) were for one isolate each of B. fragilis and B. caccae, respectively. The lowest MICs at which 50 and 90% of the isolates tested are inhibited (MIC<sub>50</sub> and MIC<sub>90</sub>, respectively) for tigecycline were observed for B. uniformis (MIC<sub>50</sub> of 1 µg/ml and MIC<sub>90</sub> of 2 µg/ml). The MIC<sub>50</sub> and other species were 8 µg/ml, with the exception of B. ovatus (MIC<sub>90</sub> of 4 µg/ml).

The results of this evaluation show that tigecycline should be considered as a possible therapeutic agent for the treatment of mixed infections, particularly intra-abdominal sepsis. Clinical trials, in progress, should establish the potential use of this drug in mixed infections.

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REFERENCES