Introduction

Delafloxacin is a broad-spectrum fluoroquinolone antibacterial that has potential clinical development interest and resistance formulations for acute bacterial skin and skin structure infections (ABSSSI) and respiratory tract infections (RTI).

The new drug application for delafloxacin was approved in 2015 by the US Food and Drug Administration in 2015 to treat acute bacterial skin and skin structure infections (ABSSSI). Delafloxacin is in phase 3 clinical development for community-acquired pneumonia (CAP) and its activity against community-acquired respiratory tract infection isolates (CARTI) was evaluated.

Materials and Methods

A total of 3,538 isolates that included 1,217 Streptococcus pneumoniae, 683 Haemophilus influenzae, and 450 Moraxella catarrhalis were collected from 2014 to 2017.

- Only 1 isolate per patient/infected episode was included.
- Isolate determinations were confirmed at JMI Laboratories.
- Susceptibility testing was performed according to CLSI reference broth (dilution antimicrobial susceptibility tests for bacteria that grow aerobically; non-meningitis breakpoints). EUCAST version 8.0 2018 was used.
- Other antibiotics tested included levofloxacin, moxifloxacin, azithromycin, clarithromycin, erythromycin, tetracycline, trimethoprim-sulfamethoxazole, and penicillin.

Results

Delafloxacin demonstrated potent in vitro activity against S. pneumoniae (MIC<0.015 mg/L) and was more active than levofloxacin (MIC<0.12 mg/L) and moxifloxacin (MIC<0.06 mg/L), as shown in Table 1 and Figure 1. Delafloxacin had the lowest MIC, which was the lowest MIC of the agents tested (Figure 1).

For 32 levofloxacin-resistant S. pneumoniae (MIC>0.12 mg/L) isolates, the delafloxacin MIC50 values were 0.004 to 0.03 mg/L, with 98.7% of the isolates having delafloxacin MIC ≤0.06 mg/L (Figure 2).

For 683 H. influenzae, delafloxacin was extremely potent, with MIC90 values of 0.03/0.002 mg/L, while levofloxacin (MIC90 values of 0.015/0.008 mg/L) and moxifloxacin (MIC90 values of 0.030/0.030 mg/L) had lower MIC values. Delafloxacin had the lowest MIC, which was the lowest MIC of the agents tested (Figure 1).

Conclusions

- Delafloxacin demonstrated extremely potent in vitro antibacterial activity against CARTI pathogens that included S. pneumoniae, H. influenzae, and M. catarrhalis.
- Delafloxacin was very active against Streptococcus pneumoniae isolates, with MIC≤0.015 mg/L and penicillin-resistant S. pneumoniae isolates (MIC≤0.12 mg/L).
- Delafloxacin inhibited all 1 levofloxacin-resistant S. pneumoniae isolates at ≤MIC50 mg/L.
- These data support the continued clinical development of delafloxacin for the treatment of community-acquired pneumonia.

Acknowledgements

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Table 2. Antimicrobial activity of delafloxacin and comparator agents tested against CARTI isolates.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC50 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Range (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>0.015/0.030</td>
<td>0.030/0.060</td>
<td>≤0.03 to &gt;4</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.030/0.060</td>
<td>0.060/0.120</td>
<td>≤0.03 to &gt;4</td>
</tr>
<tr>
<td>ERY (single agent)</td>
<td>0.030/0.060</td>
<td>0.060/0.120</td>
<td>≤0.03 to &gt;4</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.015/0.030</td>
<td>0.030/0.060</td>
<td>≤0.03 to &gt;4</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.030/0.060</td>
<td>0.060/0.120</td>
<td>≤0.03 to &gt;4</td>
</tr>
</tbody>
</table>
| M100Ed28E. Performance standards for antimicrobial susceptibility testing: 28th informational supplement.

References

