Sarecycline Demonstrates Narrow-spectrum Antibacterial Activity and Anti-inflammatory Effect in Animal Models

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Introduction

- Sarecycline is an FDA-approved tetracycline-class oral antibiotic specifically developed for the treatment of moderate-to-severe acne vulgaris.
- In vitro studies demonstrated a narrow-spectrum antibacterial activity, targeting clinically relevant Gram-positive bacteria while showing reduced activity against Gram-negative bacteria commonly found in the human gastrointestinal tract.
- Here we report results of in vivo antibacterial and anti-inflammatory studies in mouse and rat models.

Methods

In vivo antibacterial activity

Table 1. A murine systemic (intraperitoneal) infection model was utilized to assess the in vivo efficacies of sarecycline, doxycycline, and minocycline against *S. aureus* RN450-1 and *E. coli* PBS1478.

Table 2. A murine neutropenic thigh wound infection model was utilized to represent a tissue-based infection to assess the comparative efficacies of sarecycline and doxycycline against *S. aureus* RN450-1.

Anti-inflammatory effect In vivo

Table 3. To evaluate the anti-inflammatory effects of sarecycline, a carrageenan-induced rat footpad edema model was utilized. Male, Sprague Dawley rats were intraperitoneally injected with saline, sarecycline, or a positive control (doxycycline or minocycline) and inflammation was determined as change in paw volume. Percent inflammation was calculated as 100 x (post paw volume at 3 hours – pre paw volume at 0 hours)/pre paw volume at 0 hours).

Results

Results - Table 1. Efficacy of sarecycline and comparators against *S. aureus* and *E. coli* in mouse

<table>
<thead>
<tr>
<th>Antibacterial</th>
<th><em>S. aureus</em> RN450-1</th>
<th><em>E. coli</em> PBS1478</th>
</tr>
</thead>
<tbody>
<tr>
<td>agent</td>
<td>MIC (μg/mL)</td>
<td>PD50 (mg/kg)</td>
</tr>
<tr>
<td>Sarecycline</td>
<td>&lt; 0.06</td>
<td>0.25</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>&lt; 0.06</td>
<td>0.3</td>
</tr>
<tr>
<td>Minocycline</td>
<td>&lt; 0.06</td>
<td>0.03</td>
</tr>
</tbody>
</table>

MIC – minimum inhibitory concentration; PD50 – protective dose required to achieve 50% survival

Discussion

- Sarecycline is the first narrow-spectrum tetracycline-class antibiotic to be developed for the treatment of acne vulgaris.
- Sarecycline proved effective against *S. aureus* (G+ Bacteria) in both systemic and tissue-based infection models in mice. However, low efficacy was demonstrated vs. *E. coli* (G- enteric bacteria).
- The reduced activity of sarecycline against bacteria commonly found in the gut suggests reduced risk of antibiotic resistance within the GI tract microbiome.
- The anti-inflammatory effect of sarecycline in rats is similar to doxycycline and minocycline, and in agreement with sarecycline being efficacious for inflammatory moderate-to-severe acne lesions in humans.

Conclusions

- Sarecycline demonstrated in vivo efficacy against *S. aureus* but not *E. coli* in animal models of infection, in agreement with the narrower-spectrum of activity observed in *in vitro* studies.
- Sarecycline showed anti-inflammatory effect comparable to doxycycline and minocycline in the rat footpad edema model.

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