Eravacycline in vitro activity against clinical isolates obtained from urinary and gastrointestinal sources, including drug-resistant pathogens, from patients in Europe

Matteo Bassetti1, Ian Morrissey2, Trudy Grossman3, Melanie Olesky3, Hina Patel3, Joyce Sutcliffe3

1Santa Maria Misericordia Hospital, Udine, Italy; 2HIMA Gorge Sail, Gudingen, Switzerland; 3Tetraphase Pharmaceuticals, Watertown, MA, USA

Introduction
Gram-negative bacteria are a common cause of urinary and gastrointestinal infections and resistance amongst these pathogens is increasing. Eravacycline is a novel, fully synthetic fluoroquinolone antibiotic of the tetracycline class with broad-spectrum activity in development for the treatment of serious infections, including those caused by multi-resistant (MDR) pathogens. Eravacycline has been evaluated in phase I studies for the treatment of complicated intra-abdominal infections (cIAIs) and complicated urinary tract infections (cUTIs) (including pyelonephritis). The purpose of this study was to assess the in vitro activity of eravacycline against recent European clinical isolates of key pathogens from gastroenterological (GI) and genitourinary (GU) infections.

Methods
A total of 375 GI and 476 GU clinical isolates, collected from 2013-2014 from amongst 134 European hospitals, were tested.

Minimum inhibitory concentration (MIC) endpoints were determined by broth microdilution according to CLSI guidelines [1].

Quality control testing was performed each day of testing as specified by the CLSI using Escherichia coli ATCC 25922, E. coli ATCC 35218, and Enterococcus faecalis ATCC 29212. Amoxicillin-benzylpenicillin ATCC 29213, imipenem ATCC B069, Pseudomonas aeruginosa ATCC 27853, Staphylococcus aureus ATCC 29213, and Sarcina lutea ATCC 9341 were tested.

Antibiotic susceptibility was determined using EUCAST 0211 Eravacycline [2].

MIC90 was most resistant = 2 mg/L. For each of the following antibiotic classes, the following were determined: collection, the development of resistance in vitro to the antibiotics tested, and the development of resistance in vitro to the antibiotics tested.

Results
The organisms tested were comparatively distributed across European countries with predominance from France, Italy, Spain, and Belgium; 51%, 19%, 16%, 11%, and 4%, respectively. Organisms from Eastern Europe represented 26% of the total (133-193 isolates, Hungary, Poland, Romania, and Turkey).

For GI and GU isolates shown in Table 1, if the eravacycline MIC > 8 mg/L, resistant for Pseudomonas aeruginosa (ATCC 27853, S. aureus, and S. epidermidis) (0.5-4 mg/L), and sensitive for Enterobacteriaceae (ATCC 25922, S. lutea, and Enterococcus faecalis) (0.03-0.5 mg/L).

Eravacycline MIC90 was most resistant = 2 mg/L. For each of the following antibiotic classes, the following were determined: collection, the development of resistance in vitro to the antibiotics tested, and the development of resistance in vitro to the antibiotics tested.

Table 2. Categorical MIC distribution of eravacycline against peri-anal organisms for resistance phenotypes from 3 GI and 3 GU samples (where n = 10).

<table>
<thead>
<tr>
<th>Organism/Antimicrobial</th>
<th>MIC (mg/L)</th>
<th>MIC90</th>
<th>MIC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0.06-1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>0.06-2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>0.03-0.5</td>
<td>0.5</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Conclusions
Eravacycline showed activity against isolates from gastroenterological and genitourinary infections, including multi-drug-resistant and carbapenem-resistant isolates from Europe.