Multi-Locus Sequence Typing of Isolates from a Phase 2 Complicated Intra-Abdominal Trial for Eravacycline

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Multi-Locus Sequence Typing

Results

Background

The novel broad spectrum fluoroquinolones, eravacycline, and comparators etepipenem were tested in a phase 2 clinical trial assessing efficacy in the treatment of community-acquired complicated intra-abdominal infections (CAIIs) with sites in Bulgaria, India, Latvia, Lithuania, Romania, and the United States. Single Escherichia coli clinical groups, i.e., ST131, can be responsible for significant antimicrobial-resistant infections globally. The strain typing of E. coli isolates was done to determine the frequency of E. coli ST131 in patients with CAIIs in the trial.

Methods

A total of two hundred and twelve baseline isolates were collected from one hundred and nineteen patients, with E. coli as the most frequent isolate, comprising 44.3% (n=54) of all bacterial isolates in the microbiologically modified intent-to-treat population. Of these E. coli, eighty-eight individual isolates were available for evaluation of antimicrobial profile, resistance gene characterization, and multi-locus sequence type (MLST). Standard PCR methodology was used to amplify specific regions from seven independent loci: adk, fumC, gyrB, icd, mdh, purA, using the Environmental Research Institute at University College, Cork (ERI-UCC) database

Figure 1 – Eravacycline Phase 2 Baseline Species Distribution

Figure 2 – E. coli Sequence Type Distribution

Table 1 – Table 1 – Susceptibility and Molecular Profiles of Most Prevalent Sequence Types

Table 2 – Geographic Distribution of Multidrug Resistant Isolates

Conclusions

The largest share of isolates from the eravacycline phase 2 clinical trial were E. coli.

The majority of multidrug-resistant isolates was ST648 (22.7%) from India.

Multi-locus sequence typing of these isolates revealed a highly diverse population representing more than 40 unique sequence types with ST131 representing only 5.7% of the phase 2 isolates.

Screening of isolates by PCR revealed a variety of lactamase resistance genes, blαTEM, and extended spectrum β lactamase genes.

The MICmin values of eravacycline were 0.25/0.5 µg/mL, regardless of resistance phenotype and consistent with the values obtained with an even larger set of isolates (n=445).

Eravacycline was potent and efficacious across all sequence types and MDR phenotypes.

References


