Results in Higher-Risk Subgroups from IGNITE1: A Phase 3 Study to Evaluate the Efficacy and Safety of Eravacycline versus Ertapenem in Complicated Intra-abdominal Infections

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Objective

The objective of this analysis is to compare outcomes between ERV and ERT in high-risk subgroups in patients with Clostridium difficile infection (CDI).

Methods

Qualified subgroups enrolled in the study were randomized to 1 of 2 treatment groups: eravacycline 1.5 mg/kg every 12 hours (Q12H), or ertapenem every 24 hours (Q24H), in a 1:1 ratio. Randomization was stratified based on the primary site of infection (peripheral complicated appendicitis versus isolated intra-abdominal abscess). Study samples were collected within 48 hours before the first dose of study drug. Samples were evaluated on Cl End Day 14 or Day 16 at the EOT visit, which occurred within 24 hours after the end of the study drug treatment. The EOT visit, which occurred after Days 28 and 3 at the Follow-up (FU) visit, which occurred after Days 28 and 30. All subjects remained hospitalized for the complete course of drug therapy.

Background: Eravacycline (ERV) is a novel fluoroquinolone that is highly active in vitro against multidrug-resistant bacterial pathogens, including those resistant to extended-spectrum β-lactamase (ESBL). In IGNITE1, a phase 3 study, we evaluated the efficacy and safety of ERV in the treatment of C. difficile infection (CDI), which had already been reported. The results showed that ERV was superior to ERT in terms of clinical response, pathogen eradication, and adverse events. Therefore, we conducted this analysis to determine the clinical response, pathogen eradication, and adverse events in high-risk subgroups of patients with CDI treated with ERV or ERT.

Diagnosis and main criteria for inclusion: Subjects aged 18 years who were administered with a combination drug regimen containing cIAI pathogens associated with permissive infections, peritonitis due to perforation or other source of tissue infection, appendicitis, pancreatic abscess (single or multiple), including those resistant to different antibiotics, or peritonitis due to perforation of an intra-abdominal abscess.

Efficacy evaluation: This study was designed to determine non-inferiority (NI) of eravacycline 1.5 mg/kg to ertapenem 1.0 mg/kg in the treatment of C. difficile infection. The primary outcome of the study was the clinical response at the end of treatment (EOT) in the C. difficile infection (CDI) population.

Clinical outcomes evaluated: The primary outcome of the study was the clinical response at the end of treatment (EOT) in the C. difficile infection (CDI) population. The secondary outcomes evaluated included pathogen eradication, safety, and tolerability. Clinical outcomes were evaluated by the treating physician. Compliance was evaluated by the treating physician, and the primary outcome was defined as the percentage of patients with complete resolution or improvement of symptoms and signs of infection.

Results

Table 1: Baseline demographics of the patients in the microbiological ITT population

<table>
<thead>
<tr>
<th>Group</th>
<th>Gender, male (%)</th>
<th>Age, mean (SD)</th>
<th>BMI, mean (SD)</th>
<th>Body mass index (BMI), mean (SD)</th>
<th>Baseline APACHE II category (%)</th>
<th>Presence of barriers</th>
<th>Drug diabetes, percentage (%)</th>
<th>Adverse events, percentage (%)</th>
<th>Intravenous route (%)</th>
<th>Pathogen eradication</th>
<th>Wound infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>50 (30.8)</td>
<td>35—80 years</td>
<td>BMI 23.1 ± 4.8</td>
<td>BMI 26.1 ± 4.0</td>
<td>66 (%) (29.4%)</td>
<td>23% (10.8%)</td>
<td>24% (11.6%)</td>
<td>20% (9.3%)</td>
<td>76% (33.8%)</td>
<td>100% (49.5%)</td>
<td>1% (0.5%)</td>
</tr>
<tr>
<td>C. difficile infection</td>
<td>50 (30.8)</td>
<td>35—80 years</td>
<td>BMI 23.1 ± 4.8</td>
<td>BMI 26.1 ± 4.0</td>
<td>66 (%) (29.4%)</td>
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</tbody>
</table>

Conclusions

- Outcomes in patients treated with ERV were similar to those treated with ETP in adult patients with CDI. This is consistent with the results of a previous study that demonstrated a similar efficacy and safety profile of ERV in patients with CDI compared to ERT. This is important as it allows for the potential use of ERV in this complex and at-risk population.

- The analysis included patients with C. difficile infection (CDI) who were treated with ERV or ERT. The study was designed to determine the clinical response, pathogen eradication, and adverse events in high-risk subgroups of patients with CDI treated with ERV or ERT.

- The results showed that ERV was superior to ERT in terms of clinical response, pathogen eradication, and adverse events. This is consistent with previous studies that have shown ERV to be a safe and effective treatment for CDI.

- The study was conducted at multiple sites in the United States and included patients with a wide range of baseline characteristics. This allows for a more generalizable conclusion that ERV is a safe and effective treatment for CDI in high-risk subgroups.

- The study was limited by the fact that it was a retrospective analysis and the sample size was relatively small. This may limit the generalizability of the findings to a larger population.

- The study was sponsored by TelaHealth and TelaTarp enterprises. This may raise concerns about potential conflicts of interest and the potential influence of the sponsor on the results of the study.

- The study was registered with ClinicalTrials.gov (NCT01393123) and was funded by TelaHealth Pharmaceuticals.

- The study was retrospectively analyzed and the data were extracted from electronic medical records. This may raise concerns about the accuracy and completeness of the data collected.

- The study was conducted in a single-center, randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety, efficacy, and PK of cIAIs in adult patients with C. difficile infection who were treated with ERV or ERT. The study included a total of 262 patients, with 130 patients in each treatment group. The patients were randomized to receive either ERV (1.5 mg/kg every 12 hours) or ERT (1.0 mg/kg every 24 hours) for 10 days. The primary outcome of the study was clinical response at the end of treatment (EOT) in the C. difficile infection (CDI) population. The secondary outcomes evaluated included pathogen eradication, safety, and tolerability.

- The results showed that ERV was superior to ERT in terms of clinical response, pathogen eradication, and adverse events. The clinical response at the end of treatment (EOT) in the C. difficile infection (CDI) population was 100% (49.5%) for ERV and 76% (33.8%) for ERT. The pathogen eradication rate was 100% (49.5%) for ERV and 100% (49.5%) for ERT. The adverse event rates were comparable between the two treatment groups.

- The study was limited by the fact that it was a single-center study and the sample size was relatively small. This may limit the generalizability of the findings to a larger population.

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