Clinical Stability Indicators Between Ertapenem and Tebipenem Pivoxil, an Oral Carbapenem, in Hospitalized Adults with Complicated Urinary Tract Infection

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Background

• Treatment of complicated urinary tract infection (cUTI), including acute pyelonephritis (AP) due to multi-drug resistant (MDR) gram-negative pathogens (e.g., extended-spectrum β-lactamase producing and fluoroquinolone-resistant strain) is associated with poor outcomes and increased costs of care.1-3

• With many cases of cUTI, patients with UUTAP are commonly hospitalized to receive intravenous (IV) antibiotic therapy, with few oral antibiotic options available to allow clinically stable patients an opportunity to switch from IV to oral antibiotics to facilitate hospital discharge.4

• Antimicrobial stewardship guidelines advocate for an improved use of oral antibiotics, which can reduce costs and length of hospital stay.5

• Oral conversion of the same antibiotic or class is less complicated than other strategies and is applicable in many healthcare settings.6

• Antimicrobial stewardship programs often attempt to implement strategies to actively assess patients who can safely therapy on an oral regimen to reduce the need for IV catheters, associated costs and risk for adverse events, and to minimize parenteral therapy.4,7

• Tebipenem pivoxil hydrobromide (TBP-PI-HBr) is a novel, orally bioavailable carbapenem antibiotic in development for the treatment of cUTI.7-9

• The recently completed ADAPT-PO trial demonstrated the non-inferiority of oral TBP-PI-HBr versus IV ertapenem in hospitalized patients with UUTAP.7

Objective

We sought to evaluate markers of clinical stability from ADAPT-PO to assess a potential timeframe for possible efficacy and safety of oral TBP-PI-HBr vs. IV ertapenem in hospitalized adults with cUTI/AP.

Table 1. Baseline characteristics by diagnosis (micro-ITT population)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Male</th>
<th>Age at informed consent, n (%)</th>
<th>Sex, n (%)</th>
<th>TBP-PI-HBr (N=449)</th>
<th>Ertapenem (N=419)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cUTI</td>
<td>226</td>
<td>103</td>
<td>64.7 (14.8)</td>
<td>50.7 (19.7)</td>
<td>126 (56.5)</td>
<td>165 (73.0)</td>
</tr>
<tr>
<td>AP</td>
<td>201</td>
<td>101</td>
<td>66.0 (12.8)</td>
<td>50.7 (19.3)</td>
<td>102 (50.9)</td>
<td>135 (67.2)</td>
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<tr>
<td>ESBL-positive</td>
<td>126</td>
<td>64</td>
<td>66.0 (13.5)</td>
<td>50.7 (19.3)</td>
<td>64 (51.2)</td>
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<tr>
<td>ESBL-negative</td>
<td>94</td>
<td>51</td>
<td>66.0 (13.5)</td>
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Table 2. Baseline characteristics by diagnosis (micro-ITT population)

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Results

The mean time to defervescence in the IV ertapenem group was 2.2 days, at which point 65% of patients were afebrile (median 2 days in both treatment groups).10

• Time to resolution or improvement amongst patients infected with ESBL-negative and ESBL-positive strains, and patients with baseline Systemic Inflammatory Response Syndrome (SIRS).

Conclusions

The mean time to defervescence in both the IV ertapenem group and oral TBP-PI-HBr group was 2.2 days, at which point 65% of patients were afebrile (median 2 days in both treatment groups).10

• The mean time to improvement or resolution amongst patients infected with ESBL-negative and ESBL-positive strains, and patients with baseline Systemic Inflammatory Response Syndrome (SIRS).

• In this time-to-event analysis from a pivotal, Phase 3 non-inferiority trial, markers of clinical stability were similar for both randomized treatment arms.7

References

8. Takahashi K, et al. 20;10(7):1131-1140

This research was funded in part with Federal funds from DHS, ASPR, and BARDA under Contract No. HHSO100201800015C.