### Evaluation of Plazomicin (PLZ), Tigecycline (TGC), and Meropenem (MEM) Pharmacodynamic (PD) Exposure against Carbapenem-Resistant Entero bacteriaceae (CRE) in Evaluable Patients from the CARE Study (ACHN-490-007)

**OBJECTIVES**

- To develop a population pharmacodynamic model for tigecycline and meropenem using sparse samples collected for evaluation of pharmacokinetic-pharmacodynamic (PK-PD) relationships for tigecycline and meropenem during the ACHN-490-007 study.
- To assess the microbiological response of each patient with respect to pharmacodynamic exposure for plazomicin and meropenem or tigecycline.
- To assess the microbiological response of each patient with respect to the primary clinical efficacy endpoint of Cure defined as the patient being alive at Day 28 with absence of significant disease related complications (SDRC); failure was defined as death at Day 28, presence of SDRC, or both.

**METHODS**

- **Patients:** Included 18 patients: 11 for tigecycline and 7 for meropenem.
- **Methods:** Pharmacodynamic analyses were performed using sparse samples from Day 1 and end of therapy at 6 time points, Day 7 at 2 time points, and possibly on unscheduled TDM days at 2 time points following completion of the treatment period.

**RESULTS**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (MIC)</th>
<th><em><strong>AUC/MIC</strong></em></th>
<th>Response at TOC</th>
<th>Pharmacodynamic Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tigecycline</td>
<td>0.5</td>
<td>1</td>
<td>Yes</td>
<td>Positive microbiological response was observed in 13 of the 15 (86.7%) patients who achieved threshold exposure.</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1</td>
<td>2</td>
<td>Yes</td>
<td>Positive microbiological response was observed in 13 of the 15 (86.7%) patients who achieved threshold exposure.</td>
</tr>
</tbody>
</table>

**DISCUSSION AND CONCLUSIONS**

- AUC/MIC exposures were higher than the 40% predicted threshold exposure for tigecycline in all evaluated patients.
- AUC/MIC exposures were higher than the 40% predicted threshold exposure for meropenem in all evaluated patients.

**ACKNOWLEDGEMENTS**

- The authors would like to acknowledge Kristie Kooken and Alex Smith from Ad hoc Bioanalytical Support for their contributions.

**REFERENCES**

[4] AUC/MIC exposure was estimated from covariate based demographic models.