Cefepime-Taniborbactam

Addressing Current and Future Antimicrobial Resistance

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ID Week 2022

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Disclosures, Acknowledgments, and Thank You

- **Employee of Venatorx**

Special thank you to:

- **Participants/Patients of the cefepime-taniborbactam clinical program**
- **Clinical Investigators**
- **Our Partners**
  - **NIH, BARDA, Everest Medicines, GARDP, Wellcome Trust**
- **Our Employees**
  - **For discovering and developing taniborbactam**

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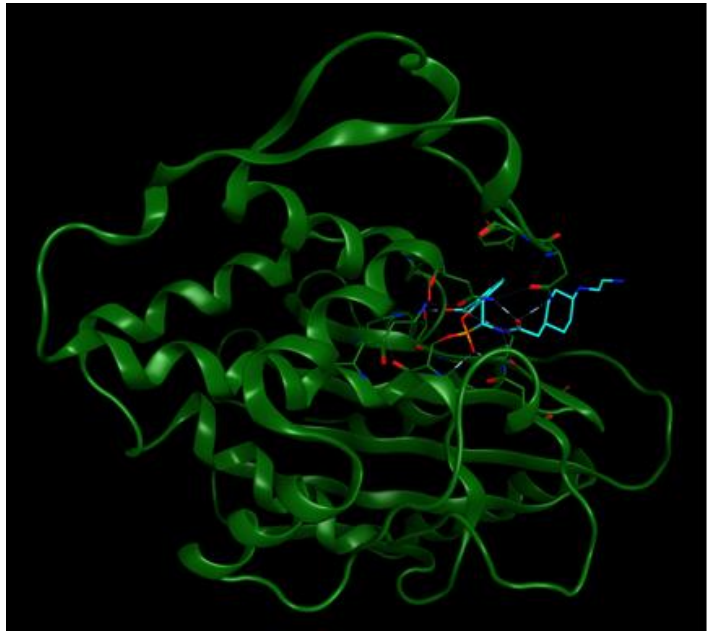
Taniborbactam – A Broad-Spectrum β-lactamase Inhibitor (BLI) with a Novel MOA

Serine β-lactamases

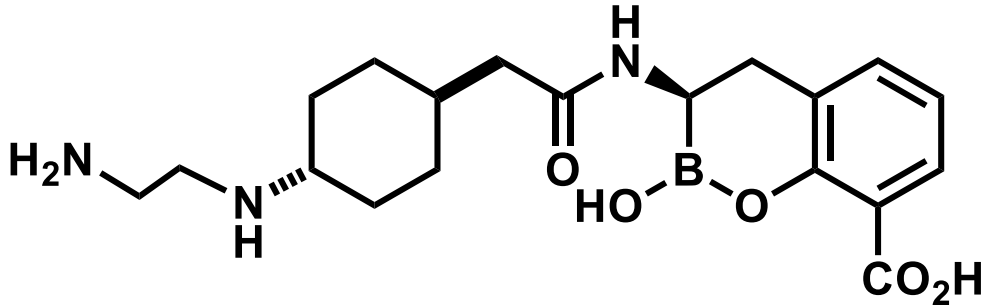
(Ambler Classes A, C, and D)



Metallo β-lactamases

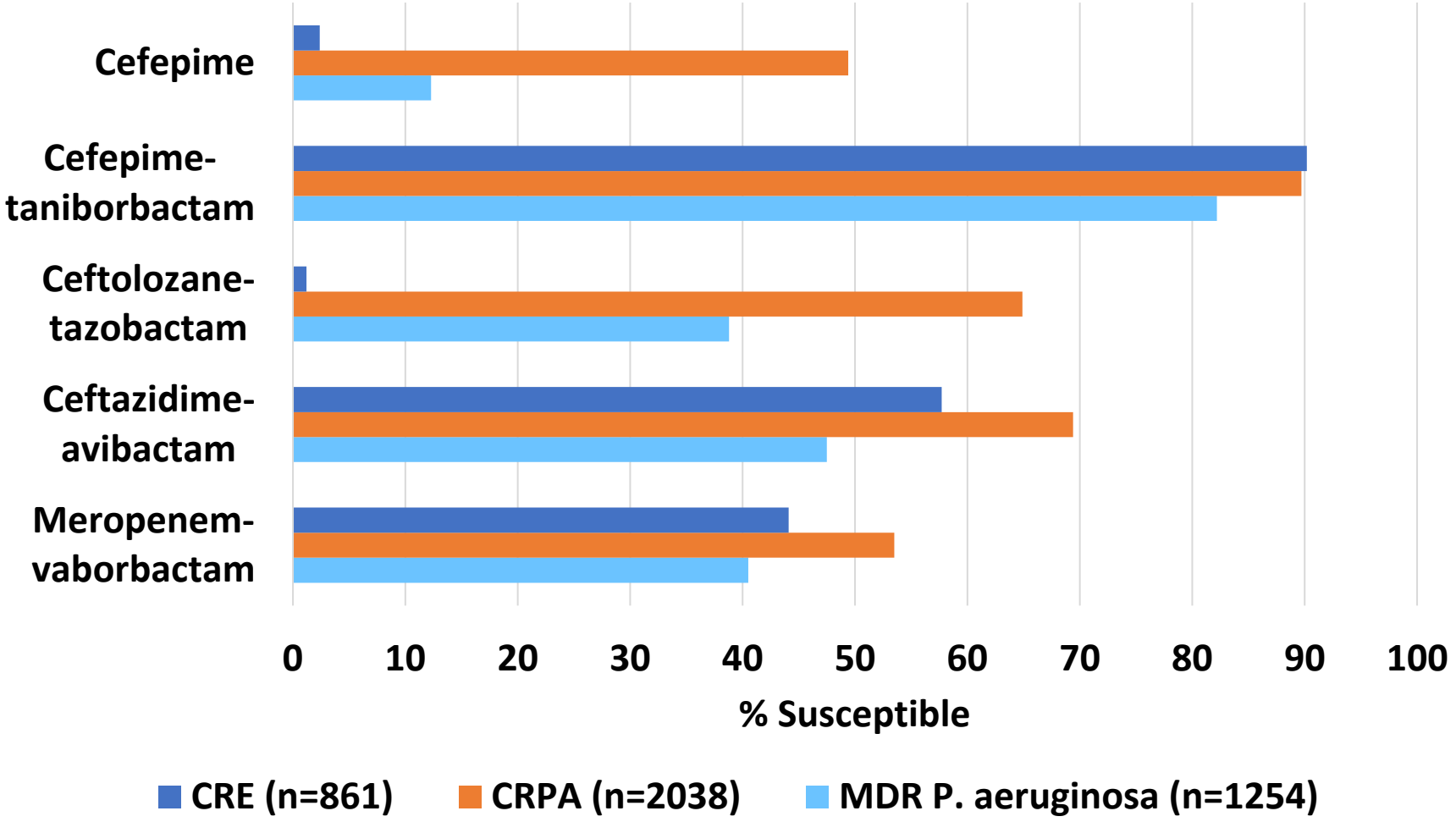
(Ambler Class B – NDM, VIM)

Taniborbactam (light blue) inhibits both enzyme types



X-ray structural data: Dr. J.D. Docquier, U. Siena, Italy

Cefepime-Taniborbactam is Active Against Resistant Enterobacterales and *P. aeruginosa* (2018-2021 Global Surveillance)



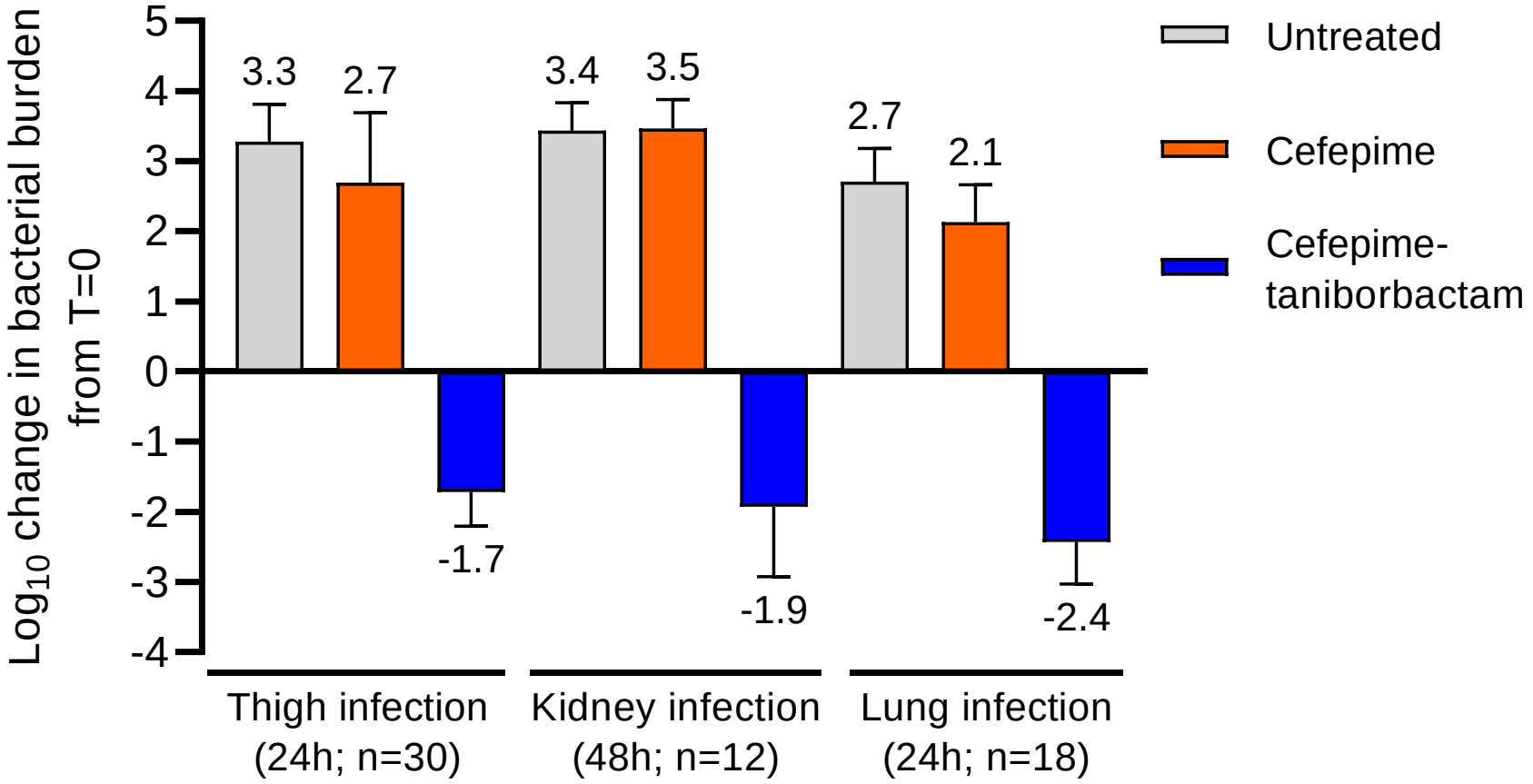
Source: IHMA global surveillance; Karlowsky et al. submitted. Provisional cefepime-taniborbactam breakpoint, S≤16 µg/mL. EUCAST breakpoint for *P. aeruginosa* used for meropenem-vaborbactam

Saturday, October 22, 2022
Exhibit Hall B/C
12:15 PM - 1:30 PM

1710 - *In Vitro* Activity of Cefepime-Taniborbactam and Comparators Against a Global Collection of Carbapenem-Resistant Enterobacterales and Carbapenem-Resistant *Pseudomonas aeruginosa* With and Without Carbapenemases
Mark Wise (IHMA)

1672 - Antimicrobial Activity of Cefepime-Taniborbactam and Comparators Against Clinical Isolates from ICU and Non-ICU Patients; 2018-2020 Global Surveillance
Meredith Hackel (IHMA)

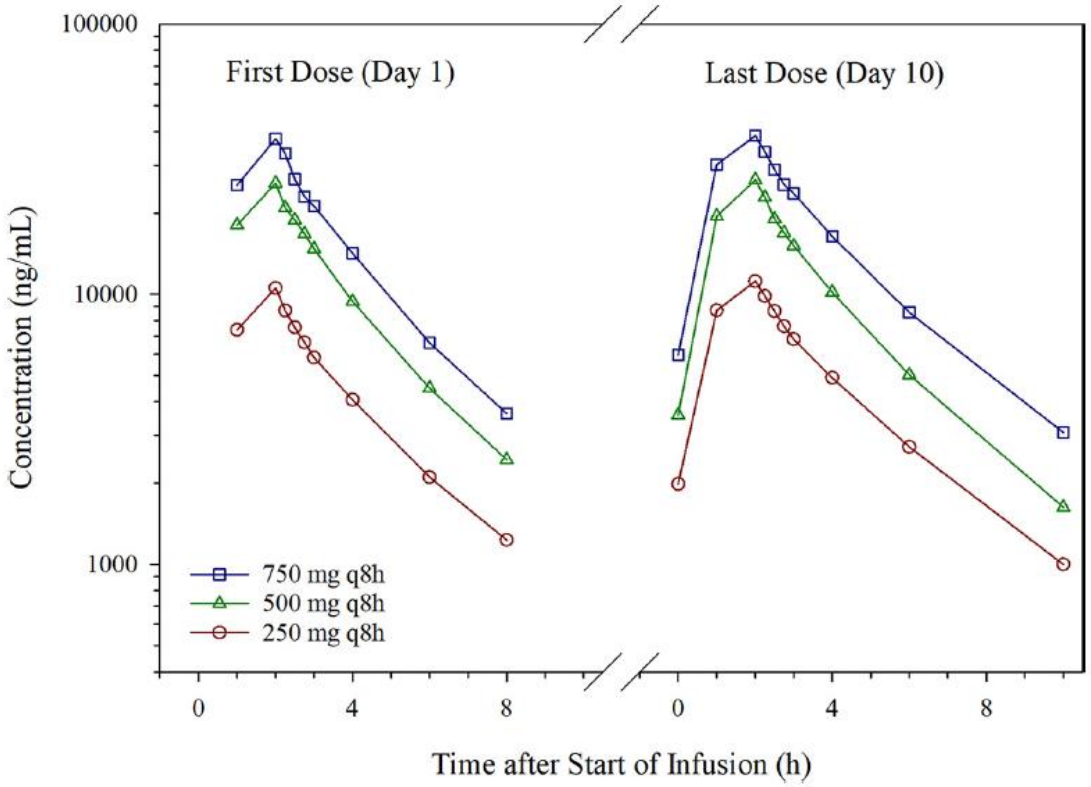
Human-Simulated Regimen of Cefepime-Taniborbactam (2 g/0.5 g) is Effective in Mouse Models of Resistant Enterobacterales and *P. aeruginosa* Infection



Cefepime-resistant clinical isolates produced combinations of ESBLs, AmpC enzymes, and serine carbapenemases.
Source: Abdelraouf et al. 2020; Lasko et al. 2022, Abdelraouf and Nicolau 2022.

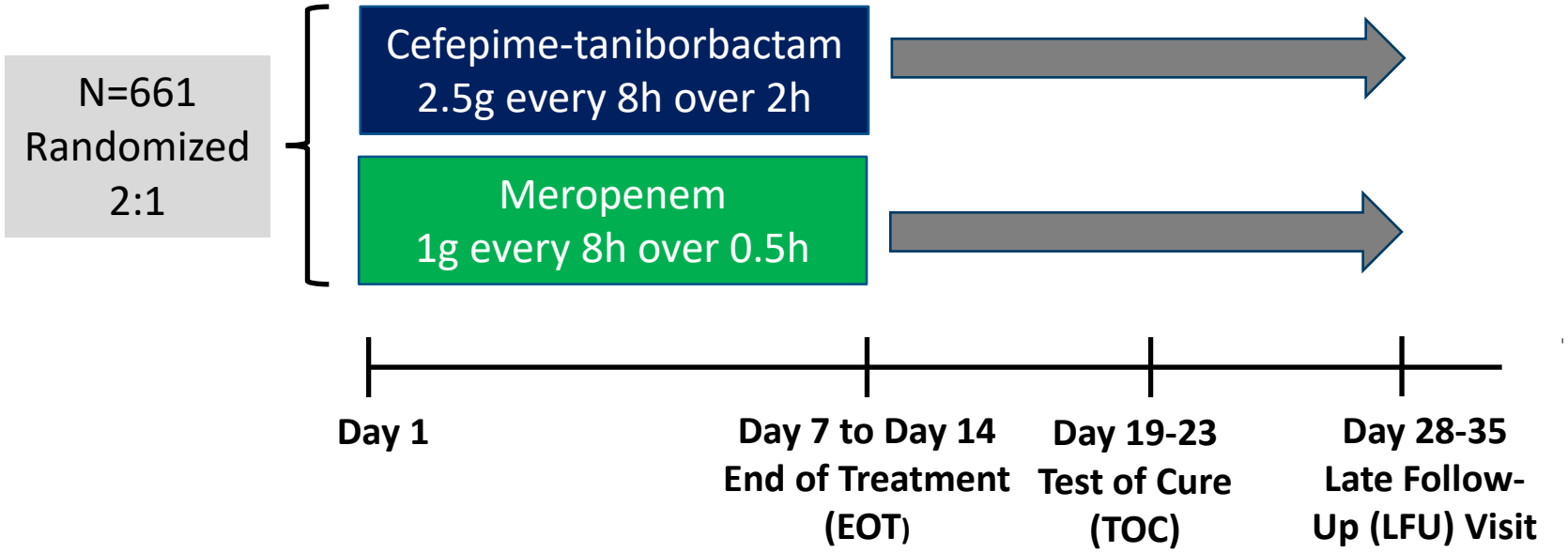
Clinical Pharmacology Profile of Taniborbactam

- **Taniborbactam exhibits dose proportional and linear PK**
  - Following single ascending doses up to 1500 mg infused over 2 hours
- **Consistent with taniborbactam's half-life (~5 hours), there is minimal accumulation (<20%)**
  - Following 2-hour infusions q8h over 10 days
- **Like cefepime, taniborbactam is extensively renally cleared**
  - ~90% of administered dose excreted in the urine
  - Cefepime and taniborbactam demonstrate ***similar and consistent*** changes in PK parameters across all renal impairment groups
- **No drug-drug interactions**
  - No hepatic metabolism in isolated hepatocytes
  - No significant inhibition/induction of CYP450 enzymes
  - Not an inhibitor or substrate of relevant transporters
- **Taniborbactam is 100% unbound in human plasma**
- **No cardiodynamic effects**

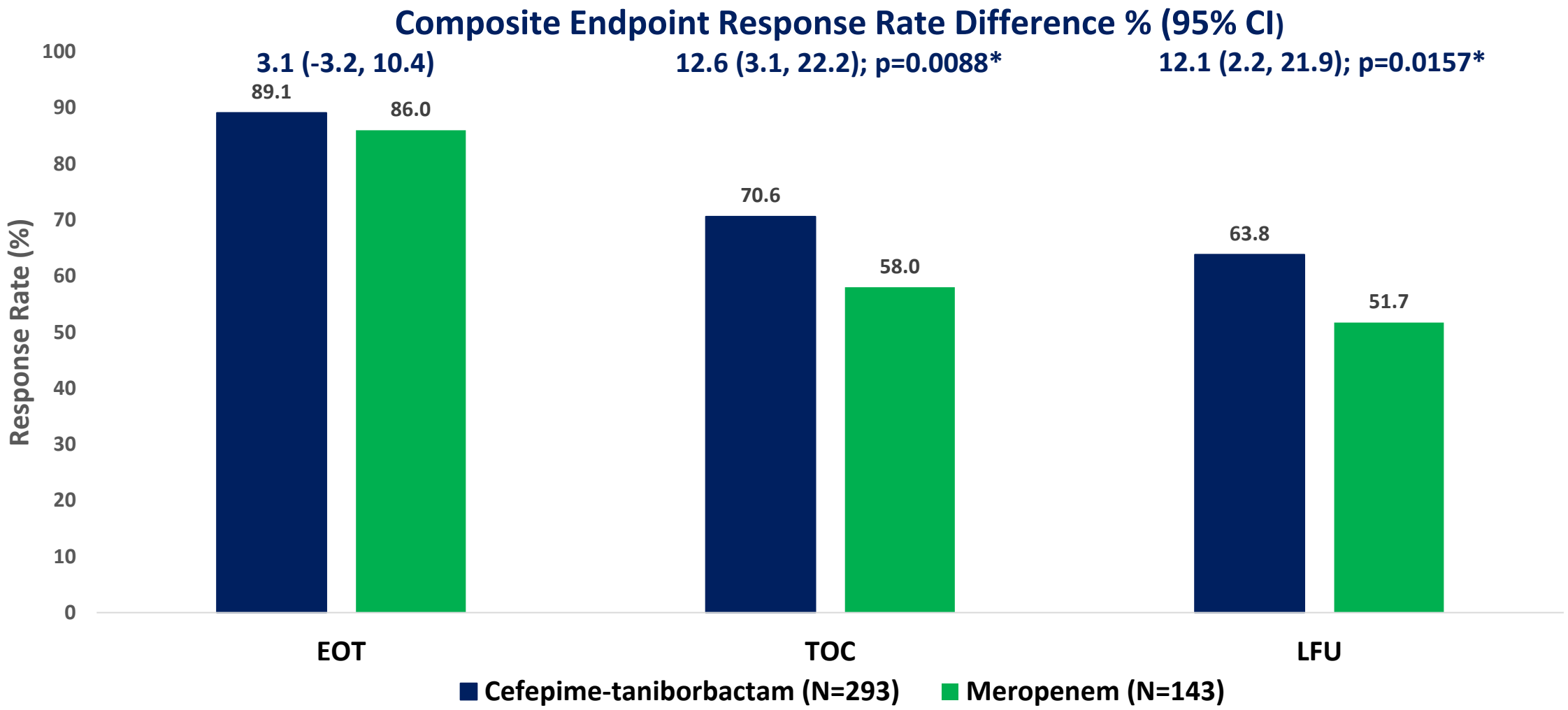


CERTAIN-1 (Cefepime Rescue with Taniborbactam in cUTI) Study Design

- **MicroITT Population (Primary Efficacy Population)**
  - Entry urine culture with gram-negative pathogen(s) at ≥10^5 CFU/mL against which both cefepime-taniborbactam and meropenem have antibacterial activity
  - No more than 2 microorganisms identified in the entry urine culture
- **Primary Endpoint – per current FDA and EMA regulatory guidance**
  - Composite microbiologic and clinical response at TOC in the microITT population
  - Non-inferiority margin set at 15%; prespecified superiority test if non-inferiority concluded



Cefepime-Taniborbactam Superior to Meropenem for the Primary Efficacy Endpoint
(microITT Population)



EOT=End of Treatment; TOC=Test of Cure; LFU=Late Follow-Up

*Statistical Superiority

CERTAIN-1 - Summary of Adverse Events (Safety Population)

	Cefepime-taniborbactam (N = 440) n (%)	Meropenem (N = 217) n (%)
Patients with At Least one TEAE*	**156 (35.5)**	**63 (29.0)**
Headache	**27 (6.1)**	**8 (3.7)**
Diarrhoea	**18 (4.1)**	**5 (2.3)**
Constipation	**14 (3.2)**	**3 (1.4)**
Hypertension	**10 (2.3)**	**2 (0.9)**
Nausea	**9 (2.0)**	**2 (0.9)**
Alanine aminotransferase increased	4 (0.9)	5 (2.3)
Patients with At Least One Serious TEAE	**9 (2.0)**	**4 (1.8)**
Patients with At Least One TEAE with Action of Drug Discontinued	**13 (3.0)**	**2 (0.9)**
Patients with At Least One Fatal TEAE	**1 (0.2)**	**0**

***TEAEs occurring in ≥ 2% in either treatment group**

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Cefepime-Taniborbactam Summary

- **Cefepime-Taniborbactam has in-vitro activity against clinically relevant resistant gram-negative pathogens including those expressing serine- and metallo-β-lactamases**
  - Extended spectrum β-lactamase producing Enterobacterales
  - Carbapenem-resistant Enterobacterales
  - Multi-drug resistant *Pseudomonas aeruginosa*
- **Superior efficacy compared to meropenem in patients with cUTI at test of cure**
  - Superiority maintained through late follow-up visit at 30 days
- **Cefepime-taniborbactam was safe and well-tolerated**
  - Low SAE rates
  - Low rate of treatment discontinuations due to TEAEs
- **NDA submission in 1H2023**
- **HABP-VABP trial beginning in 2023**

Thursday, October 20, 2022
Location: 144 ABC
2:00 PM – 2:15 PM

731 - CERTAIN-1: A Phase 3 Study of Cefepime-Taniborbactam Efficacy and Safety in the Treatment of Complicated Urinary Tract Infections (cUTI), including Acute Pyelonephritis (AP)
Paul McGovern (Venatorx)