CERTAIN-1: (Cefepime Rescue with Taniborbactam in cUTI)

A phase 3 Study of Cefepime-Taniborbactam Efficacy and Safety in the Treatment of Complicated Urinary Tract Infections (cUTI), including Acute Pyelonephritis (AP)

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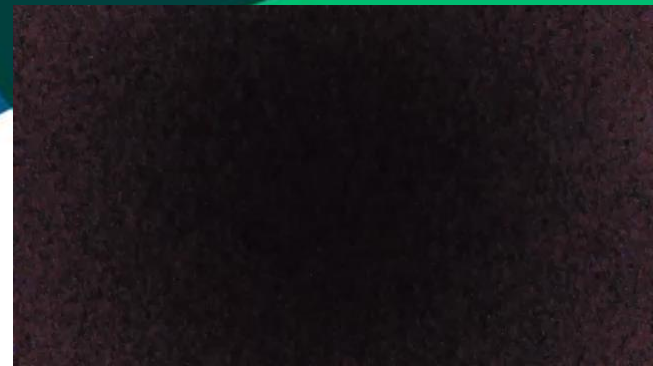
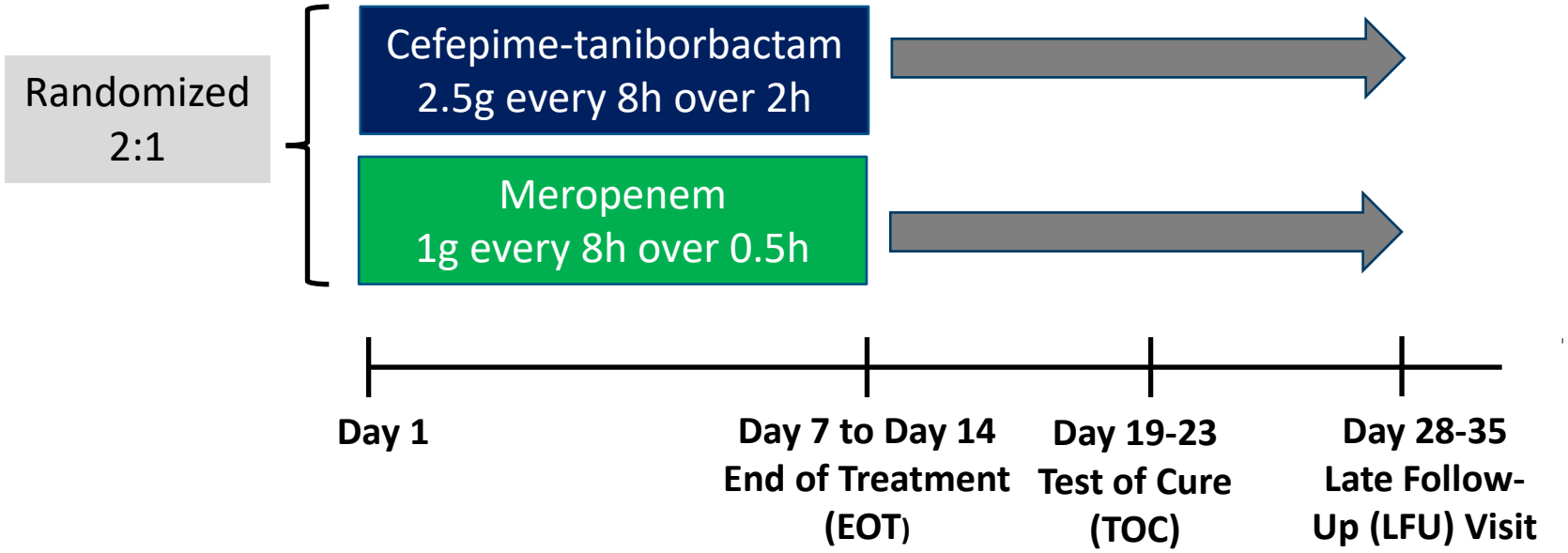


Disclosures

- **Employee of Venatorx**

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

- Randomized, multicenter, double blind, double dummy, active controlled, non-inferiority study
  - Hospitalized patients with cUTI or AP
- 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: Composite microbiologic and clinical response at TOC in the microITT population
  - Non-inferiority margin set at 15%; prespecified superiority test if non-inferiority concluded



CERTAIN-1 Randomization and Analysis Populations

661 Randomized (2:1 ratio)
Cefepime-taniborbactam N=441; Meropenem N=220

Cefepime-taniborbactam		**Safety Population**	**Meropenem**	
Included: 440 (99.8%)			Included: 217 (98.6%)	
Excluded: 1 (0.2%)			Excluded: 3 (1.4%)	
Reasons for Exclusion			Reasons for Exclusion	
Randomized not treated	1 (100%)		Randomized not treated	3 (100%)

Cefepime-taniborbactam		**microITT Population**	**Meropenem**	
Included: 293 (66.4%)			Included: 143 (65.0%)	
Excluded: 148 (33.6%)			Excluded: 77 (35.0%)	
Reasons for Exclusion			Reasons for Exclusion	
No GN pathogen ≥10^5 CFU/mL	130 (87.8%)		No GN pathogen ≥10^5 CFU/mL	67 (87.0%)
No antibacterial activity*	13 (8.8%)		No antibacterial activity*	1 (1.3%)
No susceptibility results	5 (3.4%)		No susceptibility results	8 (10.4%)
More than 2 organisms	4 (2.7%)		More than 2 organisms	1 (1.3%)

GN=gram negative; *resistant to at least one study drug

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Demography and Baseline Characteristics (microITT Population)

	Cefepime-taniborbactam (N = 293) n (%)	Meropenem (N = 143) n (%)	Total (N = 436) n (%)
Age (years), Mean (s.d.)	**56.5 (17.6)**	**55.8 (17.9)**	**56.2 (17.7)**
Age Categories (years), n (%)			
<65	180 (61.4)	90 (62.9)	270 (61.9)
65 - 75	72 (24.6)	35 (24.5)	107 (24.5)
>75	41 (14.0)	18 (12.6)	59 (13.5)
Gender, n (%)			
Male	132 (45.1)	74 (51.7)	206 (47.2)
Female	161 (54.9)	69 (48.3)	230 (52.8)
Renal Status (eGFR mL/min/1.73m^2), n (%)			
Normal (eGFR ≥ 90)	67 (22.9)	27 (18.9)	96 (22.0)
Mild impairment (eGFR 60 to <90)	137 (46.8)	77 (53.8)	212 (48.6)
Moderate impairment (eGFR 30 to <60)	84 (28.7)	38 (26.6)	122 (28.0)
Diagnosis, n (%)			
AP	126 (43.0)	58 (40.6)	184 (42.2)
cUTI	167 (57.0)	85 (59.4)	252 (57.8)
Prior antibiotics within 72 hours of treatment	**19 (6.5)**	**12 (8.4)**	**31 (7.1)**
Bacteremia, n (%)	**38 (13.0)**	**19 (13.3)**	**57 (13.1)**
Met SIRS Criteria	**70 (23.9)**	**36 (25.2)**	**106 (24.3)**
Diabetes	**49 (16.7)**	**24 (16.8)**	**73 (16.7)**

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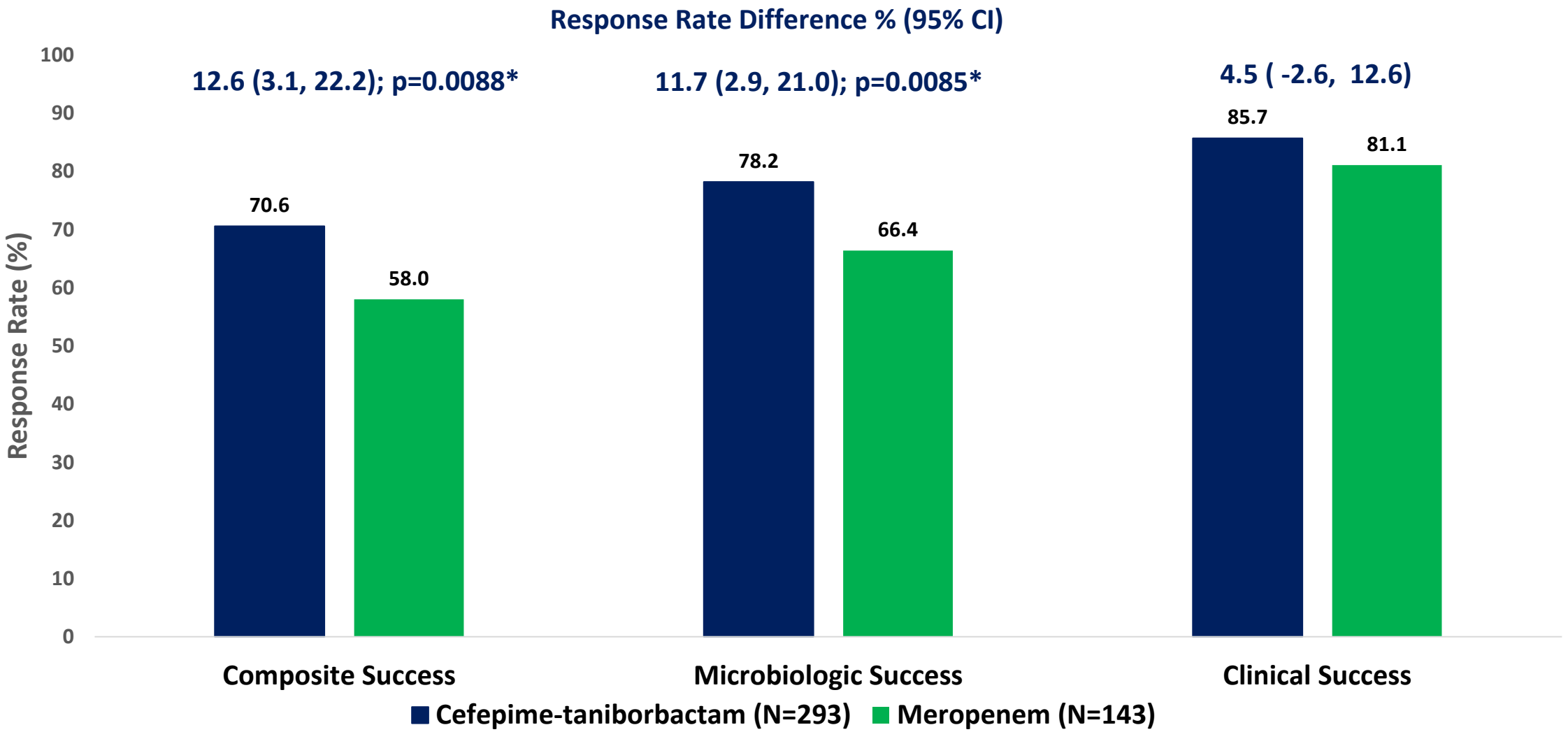
Baseline Microbiology (microITT Population)

	Cefepime-taniborbactam (N = 293) n (%)	Meropenem (N = 143) n (%)	Total (N = 436) n (%)
Monomicrobial gram-negative infection	**287 (98.0)**	**138 (96.5)**	**425 (97.5)**
Polymicrobial Infection	**6 (2.0)**	**5 (3.5)**	**11 (2.5)**
Enterobacterales	**281 (95.9)**	**137 (95.8)**	**418 (95.9)**
Enterobacter cloacae complex	14 (4.8)	3 (2.1)	17 (3.9)
Escherichia coli	202 (68.9)	99 (69.2)	301 (69.0)
Klebsiella pneumoniae	40 (13.7)	20 (14.0)	60 (13.8)
Proteus mirabilis	10 (3.4)	10 (7.0)	20 (4.6)
Pseudomonas aeruginosa	**12 (4.1)**	**6 (4.2)**	**18 (4.1)**
Cefepime-resistant pathogens	**65 (22.2)**	**30 (21.0)**	**95 (21.8)**
ESBL-producing pathogens	**80 (27.3)**	**42 (29.4)**	**122 (28.0)**
MDR pathogens	**100 (34.1)**	**56 (39.2)**	**156 (35.8)**

Cefepime-resistant pathogens defined per CLSI criteria; ESBL – Enterobacterales with ceftazidime and/or aztreonam and/or cefepime MIC ≥2 µg/mL; MDR pathogens are non-susceptible to at least one agent in three or more categories of antibacterial agents.

Cefepime-Taniborbactam Superior to Meropenem for the Primary Efficacy Endpoint

(Test of Cure Visit, MicroITT Population)



*Statistical Superiority

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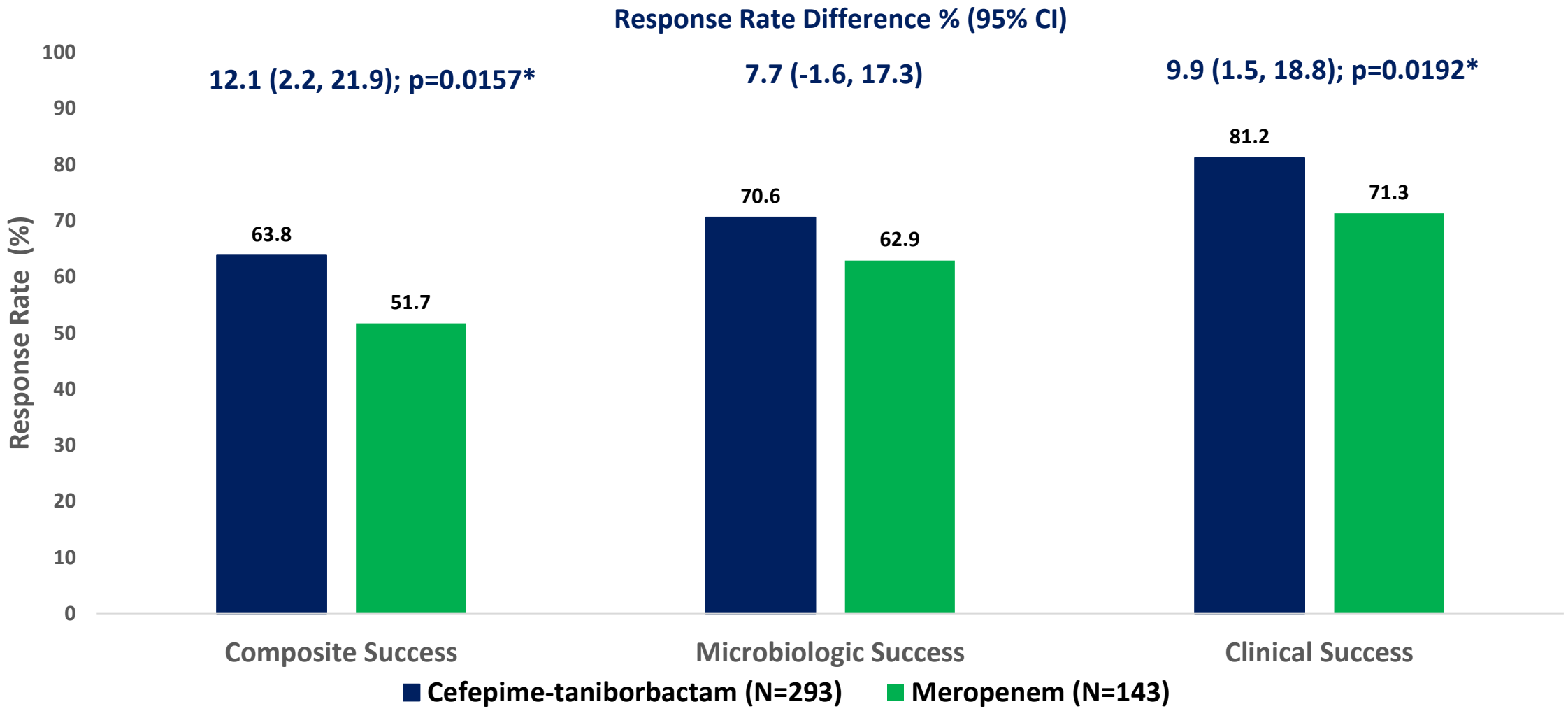
Cefepime-Taniborbactam Remains Superior to Meropenem at Late Follow-Up Visit
(microITT Population)



*Statistical Superiority

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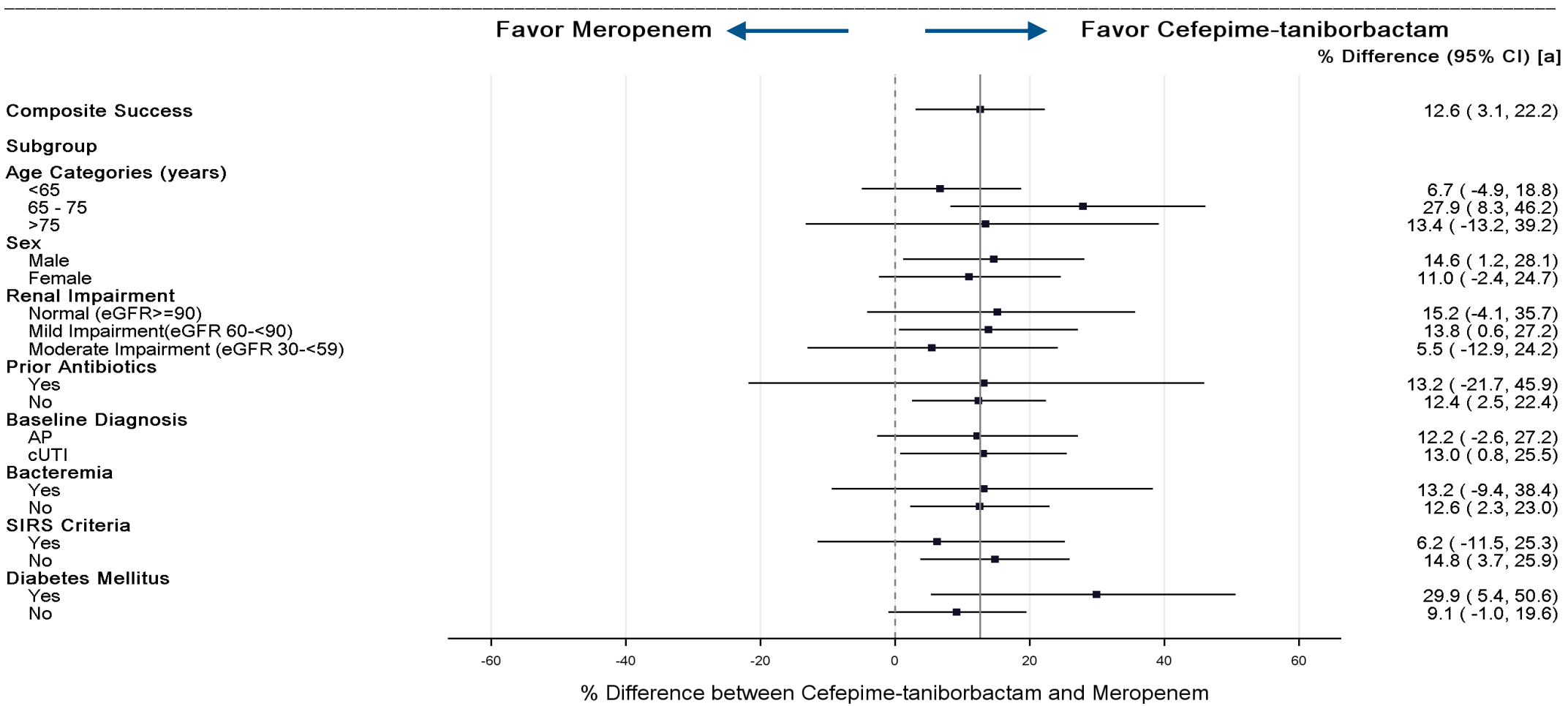
Composite Endpoint Subgroup Analysis Consistent with Primary Endpoint
(microITT Population)



[a] 95% confidence intervals of between-treatment response rate differences are based on Miettinen and Nurminen method

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Test-of-Cure | Composite Endpoint By Pathogen (microITT Population)

	Cefepime-taniborbactam n/N (%)	Meropenem n/N (%)
Enterobacterales	**202/281 (71.9)**	**80/137 (58.4)**
Enterobacter cloacae complex	11/14 (78.6)	1/3 (33.3)
Escherichia coli	147/202 (72.8)	58/99 (58.6)
Klebsiella pneumoniae	24/40 (60.0)	12/20 (60.0)
Proteus mirabilis	8/10 (80.0)	4/10 (40.0)
Pseudomonas aeruginosa	**5/12 (41.7)**	**3/6 (50.0)**
Cefepime-resistant pathogens	**46/65 (70.8)**	**16/30 (53.3)**
ESBL-producing pathogens	**55/80 (68.8)**	**24/42 (57.1)**
MDR pathogens	**67/100 (67.0)**	**33/56 (58.9)**

In the extended microITT population (susceptibility to at least one drug), cefepime-taniborbactam cured 7/8 carbapenem-resistant Enterobacterales (87.5%) and 1/2 (50%) carbapenem-resistant *P. aeruginosa* with a cefepime-taniborbactam MIC ≤ 16 mg/mL.

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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)**
TEAEs Occurring at > 2% of Patients in Either Treatment Group		
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 Withdrawn	**13 (3.0)**	**2 (0.9)**
Patients with At Least One Fatal TEAE	**1 (0.2)**	**0**

CERTAIN-1 Results | Key Takeaways

- Cefepime-taniborbactam met the prospectively defined primary endpoint of composite microbiologic and clinical response at TOC in the microITT population, demonstrating non-inferiority to meropenem
  - The lower bound of the 95% CI exceeded zero.
    - Demonstrated **Statistical Superiority** to meropenem for the composite primary endpoint at TOC visit (Day 19-23)
    - Sustained **Statistical Superiority** to meropenem for the composite endpoint at LFU visit (Day 28-35)
- Favorable safety profile similar to meropenem
  - Low rates of SAEs and treatment discontinuations
  - No safety concerns observed
  - Safety profile consistent with the meropenem comparator
- Data from CERTAIN-1 supports the registration of cefepime-taniborbactam for cUTI, including pyelonephritis
  - NDA to be filed in 1H2023

Thank You and Time for Questions

- Patients and Clinical Investigators
- External Partners
  - BARDA
  - Everest Medicines
  - GARDP
- CERTAIN-1 Study Team
- CRO – Labcorp
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